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MEDICINE AND AIR SUPREMACY*

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GEORGE CHEYNE SHATTUCK, the younger (1813–93), whose father, George Cheyne Shattuck, the elder (1784–1854), left the bequest that led to the founding of this lectureship, died early in 1893, and Osler,[1] who gave the fourth lecture of the series in that year, chose for his subject "Tuberculous Pleurisy," a theme in which the younger Shattuck had been interested since his early days in Paris, when he studied under the great French clinician, Louis. Shattuck's son, Frederick Cheever Shattuck (1847–1929), was, like his father and grandfather, a great force in New England medicine. The Shattucks were men of humor, forthright candor and passionate loyalty to the traditions of this country. Their humor is well illustrated in a lively encounter between Frederick Cheever Shattuck and Harvey Cushing, who gave the Shattuck Lecture in 1913.[2] Dr. Shattuck had read Cushing's account of the Western Reserve and its traditions,[3] and was horrified to find the word tomahawk misspelled. Dr. Cushing, his secretariat and the Cleveland proofreaders had all passed "tommyhawk"—spelled like "tommy-gun." This was too much for Frederick Cheever, who immediately commandeered conveyance to the Peter Bent Brigham Hospital, and, wearing a pair of enormous plus fours, dashed in the side door of Dr. Cushing's office to tell him that the Moseley Professor of Surgery, who had been born in the Western Reserve out among the Indians, should know the spelling of tomahawk; not content with this, he wrote Cushing a letter referring him to the *Century Dictionary*.

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I have said that the Shattucks were men of intense loyalty to this country's traditions, and when your committee requested aviation medicine as the subject of this discourse, it seemed obviously a theme wholly appropriate for a lecture devoted to the memory of this remarkable line of American physicians; moreover, a topic with military implications is not without precedent, for just twenty-five years ago,—in June, 1917,—Dr. Walter B. Cannon gave a Shattuck Lecture on traumatic shock.[4] In accepting the honor, I have, however, taken on a heavy responsibility, and one that for various reasons is embarrassing.[5]

The National Research Council and the Office of Scientific Research and Development have followed the policy of classifying as "confidential" or "secret" all topics having to do with offensive instrumentalities of war. The airplane is clearly such an instrumentality, as are many of the devices within the plane designed to improve the performance of the pilot in his rapid, high-altitude maneuvers; so that medicine, perhaps for the first time in its history, has come to be divided, so far as war is concerned, into offensive and defensive spheres. Advances that have to do with increasing the effectiveness of human performance in combat become military secrets, and cannot now be openly discussed. Defensive measures, on the other hand, designed for treating the wounded, either civilian or military, or for prophylaxis, as by inoculation, fall into the category of defensive measures and can be freely described. Aviation medicine falls squarely across the broad categories of offense and defense, and I am therefore obliged to devote attention primarily to the defensive phases of the subject.

It has become obvious, even to the most casual observer, that air supremacy will determine the outcome of the present war. Shipping still has vast importance and we look carefully to our tonnage, but all the ships of the United Nations would become virtually useless without command of the air. Supremacy in aviation is not wholly a question of more and faster planes with greater firing power than the enemy. This, to be sure, is important, but equally so is the problem of securing

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well-selected, well-trained and adequately protected flying personnel. The performance of modern aircraft has far outstripped the physiological limitations of the pilot. The newer combat planes can fly higher than is compatible with life, even when the fliers are breathing pure oxygen. They can perform maneuvers causing centrifugal force of such intensity that blood tends to be drawn away from the brain, a condition that results in transient blindness (blacking-out) and unconsciousness. And, finally, the range of the modern four-motored bombers — some of which can remain for twenty-four hours in the air — has raised problems of pilot fatigue, severe stresses and strains from cold, psychological tension and loss of sleep that impair the performance of flying personnel. It is the responsibility of medicine in its broadest sense, including psychology, psychiatry, physiology and the special branches of clinical medicine, to protect flying personnel from these and many other hazards that they face. The role of the physician in both the offensive and defensive phases of the war effort has therefore become increasingly vital for broad military strategy.

Air supremacy involves not only flying personnel but ground personnel. It is estimated that for every man in the air there are nine or ten men on the ground, both in civilian airlines and in military aviation; men on the ground are as essential as the men in the air, and if the Army should wish 100,000 pilots it must recruit 1,000,000 men. Air supremacy also extends to the men in the aircraft factories, who are exposed to special hazards peculiar to aircraft production. I cannot speak of industrial hazards in aircraft plants, but they are real and their successful handling rests with industrial physicians. In an aviation plant recently visited, 600 from a total of 30.000 employees were treated daily for accidents or illness occurring in the plant — that is, 2 per cent of the total personnel became ill or were injured each day. This is far higher than one would wish or anticipate, and yet with the vast expansion of the past twelve months, such injuries are to some extent inevitable. In a plant that is not expanding, injury rates diminish, but usually only as rapidly as the measures taken for their prevention. The need for industrial physicians in all phases of the war effort continues to be enormous.

To give a more general idea of the scope of aviation medicine, I shall describe a classified bibliography of the subject that is now in the process of publication.

Literature of Aviation Medicine

In recent months, my associates, Dr. and Mrs. Ebbe C. Hoff, and I have had the responsibility of searching out, listing and classifying all available literature bearing on the medical aspects of aviation. The project was proposed nearly eighteen months ago, and the labor is now completed, for the bibliography will be published within a few weeks.[6] The subject matter covers a vast range, the principal topics being indicated by the main chapter headings of the bibliography:

1. History and General Aspects of Aviation Medicine.
2. The Special Physiology of Aviation. (This section is divided into nineteen subsections including all the organ systems and special senses.)
3. The Special Pharmacology of Aviation.
4. The Special Psychology of Aviation.
5. Aeromicrobiology. (Bacteriology and immunology in aviation and high altitudes.)
6. Diseases and Accidents in Aviation and Conditions Simulating Flight.
7. Selection and Assessment of Efficiency of Flight Personnel.
8. Training, Performance and Fatigue of Flight Personnel.
9. Protection of Flight Personnel: Preventive medicine and therapeutics of aviation.
10. Aviation and Public Health.
11. Organization of Aviation Medicine.
12. Special Problems.
13. General Studies in Aviation Medicine.
14. Bibliographies.

It may be of interest that, although approximately six thousand separate items were found, the author index contains some nineteen thousand names, from which one must infer that those who write on the subject generally write in trios. And this expresses what some of us had gradually come to realize: that research endeavor in this field is inevitably co-operative. The flight surgeon uses a pilot or some fellow flight surgeon as a subject of an experiment, sometimes in the air, sometimes in a decompression chamber and sometimes in a human centrifuge. When decompression experiments are involved, five or six people generally constitute a team, and their names may appear as co-authors of the report.

The bibliography itself cuts across the scientific periodical literature of all pha countries, articles from abou nals having been cited. Of are medical journals.

In passing, one may mention that standpoint it would be impossible of this sort if one restricted a worked out purely for medical journals. On this point, we were fortunately forewarned and at the start adopted the conventions of *A World List of Scientific Periodicals*[7] as a basis for abbreviations; this made possible the ready citation in conveniently abbreviated form of any scientific journal in any language, without serious confusion.

In surveying this literature, we were impressed by the large number of Japanese articles on aviation medicine. Much more striking, however, was the

fact that about thirty Russian journals were represented in the bibliography, embodying a vast and well-co-ordinated literature on the subject — far ahead, incidentally, of that of Japan.

There is a widespread feeling that bibliography is a dull preoccupation reserved for spinsters and old maids of the male sex. Actually, it is far from that, for careful analysis of the literature of any subject reveals trends of research, and in the bibliography under consideration, it has exposed trends and emphasis of far-reaching international significance. The Germans, for example, began publishing papers on the effects of high acceleration in aircraft five years before the flight surgeons of the United Nations had given any general consideration to the problem, and everyone must realize what the dive bomber has meant to the Axis war effort. For better or for worse, the Allies have depended largely on horizontal bombing, but with our fast fighters we are quickly learning the significance of high acceleration, and are studying the modes of counteracting its effects on aircraft personnel.

Problem of Anoxia

The responsibility of carrying on research in the more academic phases of aviation medicine falls largely to the civilian laboratories, although one looks forward to research institutes within the military services that will continue with active investigative endeavor in times of peace. But in the present war crisis, it is clearly up to the civilian scientists to undertake the long-range problems, and in aviation medicine the most basic of these is a study of the adjustments of the body to anoxia. There are many aspects of the problem as yet imperfectly understood, — individual variations, variations of the individual, — factors that aid the body in making the adaptations, all of which involve fundamental physiological, biochemical and endocrinological research; the aim in view is to increase knowledge of the processes involved and to search out ways of improving human performance in the higher altitude ranges. To use the language of aviation, the basic problem is to raise the aviator's "ceiling." But from the purely academic standpoint, we wish first to extend our knowledge of the processes involved.

In his excellent monographic review on the effects of anoxia in the body, Van Liere[8] gives a broad picture of the manifold changes that occur when the body is exposed to low oxygen partial pressure. In adjusting, for example, to a fall of half an atmosphere, giving an equivalent altitude of 18,000 feet, there is a veritable ionic cataclysm between blood and tissues and renal tubules, accompanied by a shift of the blood pH to the alkaline side, with an extensive loss of sodium and chloride ions in the urine. Van Liere, however, makes little attempt to elucidate the important problem of how these ionic shifts are integrated. What organ responds in the first instance to the lowered oxygen partial pressure? From the work of Cannon[9] and of Gellhorn and his collaborators,[10, 11] it is known that the sympathetic system is exquisitely sensitive to anoxia and that many of the adjustments arise from the direct stimulating action of low oxygen tension on the central neurons of the sympathetic system. From the sympathetic comes the reflex mobilization of idle red blood cells from spleen, bone marrow and other reservoirs, and a vast series of vasomotor readjustments designed to improve the circulation of vital organs is brought about, also reflexly, through interaction of the sympathetic and parasympathetic systems. No one, however, appears previously to have suggested that the ionic shifts essential for anoxic acclimatization are likewise mediated through reflex channels. The evidence to date is incomplete, but suggestive, and it turns largely on recent developments bearing on the part played by the adrenocortical hormone in anoxia.

Anoxia and Adrenal Cortex

Two papers published by French flight surgeons at the end of the last war suggested that the asthenia that certain aviators developed after repeated missions to high altitudes was due to adrenal insufficiency. Ferry[12] observed urinary retention of nitrogen and alkali, low blood pressure and pathological heart sounds in a group of overfatigued aviators, and he was led on the basis of these findings to the conclusion just mentioned. The paper of Josué[13] was based on a study of physiological and psychological alterations in fatigued pilots. But since at that time there was no clear distinction between the adrenal medulla and the cortex, the suggestion can remain only of historical interest. More recently, Armstrong and Heim[14] found on exposing rabbits for four hours a day to an atmosphere equivalent to 18,000 feet that, in the early stages, hypertrophy of the adrenal gland resulted and was followed later by degenerative changes in the adrenal cortex. In his well-known book on aviation medicine, Armstrong[15] later pointed out that overfatigued pilots, especially those subjected to many high-altitude missions, developed symptoms strikingly similar to those seen in early Addison's disease.

Sundstroem,[16, 17] whose early studies on the adaptation of man to high altitudes are well known, was led some years ago to study the relation of the adrenal glands to acclimatization

and, independently of Armstrong and Heim, confirmed the existence of adrenal hypertrophy resulting from anoxia; in his monograph about to appear from the University of California Press, he[18] shows that the degree of adrenal hypertrophy can be roughly correlated with the extent to which the oxygen partial pressure is diminished. All animals exposed to diminished atmospheric pressure during the period of acclimatization tend to lose weight. This loss of weight is shared, according to Sundstroem, by all organs of the body except the adrenal cortex (and possibly the kidney); the adrenal hypertrophy is therefore regarded as something specific to the anoxic state. On the basis of the hypertrophy, Sundstroem asked himself whether this might not indicate increased secretion of the glands. He set out to obtain a direct answer to the question in two ways. In the first place, adrenal steroids were extracted from tissues, such as the heart and liver, from control animals at sea level and from groups exposed to the high-altitude ranges; the tissues of the latter animals invariably showed a larger proportion of adrenal steroid than the corresponding tissues in animals at sea level.

More impressive, however, was the study of Giragossintz and Sundstroem,[19] in which it was found that adrenalectomized animals could not survive in the high-altitude ranges and that it took twenty times more crude extract of the adrenal cortex to maintain rats at 20,000 feet than it did at sea level. This clearly suggested that to maintain the body at high altitude increased secretion of adrenocortical extract is essential.

The problem has recently been taken up anew in my laboratory by Langley and Clarke,[20, 21] who have confirmed the fact that adrenal hypertrophy develops in rats exposed to 20,000 feet; and in adrenalectomized animals, they find that at sea level the maintenance dosage for an average adult rat is 0.5 cc. of total extract a day (Wilson), or 0.03 mg. of desoxycorticosterone acetate. At 20,000 feet, a rat on this maintenance dose rapidly loses weight and dies, and Langley and Clarke find that 2 or 3 cc. of total extract is essential at that altitude and that 1 mg. of desoxycorticosterone is required. When acclimatization has taken place, however, after one week at 20,000 feet, the maintenance dose can be reduced to the sea-level amount.

Langley found, as had Gerald Evans,[22, 23] that exposure of a fasting rat to an altitude of 20,000 feet for twenty-four hours causes an elevation of both the blood-sugar and liver-glycogen levels. This suggests that Compound E, the carbohydrate fraction of the adrenocortical secretion, is mobilized in conditions of anoxia. But the desoxycorticosterone fraction appears also to be mobilized, since Langley has found in dogs exposed to an altitude of 20,000 feet that a marked increase occurs in sodium and chloride and also in potassium excretion. Following adrenalectomy, dogs subjected to anoxia failed to show the sodium and chloride excretion, although potassium loss continued. The failure of the sodium, chloride and carbohydrate adjustments in adrenalectomized animals exposed to anoxia indicates that the presence of adrenal extract is apparently essential to make the bodily adjustments to altitude, and one naturally wishes to know how the adrenal cortex is specifically activated — whether directly by the blood stream, or in some way through the nervous system. Langley,[20] in discussing the question, remarks: "It is possible that the increase in sodium chloride and urine volume observed in the normal animal exposed to anoxia was brought about by increased excretion of these specific fractions [desoxycorticosterone] of the adrenal cortex. This observation suggests that the adrenal cortex is capable of secreting certain components of the whole extract independently of the others."

The recent important work of Dr. George Thorn,[24] the newly appointed Hersey Professor of Medicine at the Harvard Medical School, has also established in animals that a large increase in sodium, chloride and potassium excretion occurs on exposure to anoxia, and he has found conspicuous nitrogen retention in man under these conditions. Treatment of adrenalectomized animals with the so-called "carbohydrate-regulating" factor caused a striking increase in sodium, chloride and water excretion, but no increase in potassium. Thorn and his collaborators[25–27] have just given an account of the effect on rats, rabbits and dogs of intermittent exposure to altitudes equivalent to 18,000 and 27,000 feet. They have confirmed Armstrong and Heim's[14] observation that adrenal hypertrophy develops in consequence of such repeated exposure in rabbits (and also rats); they have found, moreover, that the adrenalectomized animal fails to survive repeated "flights" to these altitudes, and that their capacity for adjustment can be restored by administration of adrenocortical hormone.

From the studies of Collip[28] and his students, it appears probable that the adrenal cortex is normally activated, not by the blood stream directly, but rather by the adrenotropic hormone of the anterior pituitary. The ingenious work of Uotila[29, 30] indicated that the thyrotropic hormone is under the direct control of nerve centers in the hypothalamus whose axons passed down the pituitary stalk, and that the reaction to cold results from thermal stimulation (via the blood) of the hypothalamic centers. Since the adrenal cortex also plays a large part in the reaction to cold and to anoxia, it is likely that the primary activation of the adrenal cortex comes from the hypothalamus through the adrenotropic hormone. Favoring this is the fact, originally disclosed by Gerald Evans[22] and recently confirmed by Catchpole,[31] that the chronically hypophysectomized rat has

no greater altitude tolerance than the adrenalectomized animal.

All this brings one to a far clearer concept of the mode of integration of the bodily adjustments to altitude. The part played by the respiratory center in the medulla has long been recognized. Mobilization of red cells and the reflex adjustments of the heart and circulation arise in part from direct stimulation of the chemoreceptors of the carotid body, as well as from the direct effect of low-oxygen tension on the sympathetic system; there appears to be further reflex control, through the centers in the hypothalamus, of the ionic pattern and carbohydrate level of the blood. Undoubtedly, when the complete picture has been put together, the posterior pituitary gland will also be found to play a part in these adjustments through the influence of its antidiuretic hormone on the kidney tubules. This strongly suggests that the bodily adjustments to anoxia are in large measure integrated by the central nervous system.

Safety in Crashes

The military phases of aviation medicine are rigidly practical. General academic research is encouraged at some of the larger bases and institutions, but for the immediate purposes of the war effort a group of practical problems has arisen for which solution is required in a matter of months. Combat fliers, for example, are constantly exposed to rough landings under blackout conditions, or to crash landings when machines are disabled, and the question arises whether mechanical factors for safety, similar to those introduced within the past few years in automotive design, cannot be adapted to aircraft. This raises the question of the factors responsible for injuries, fatal and otherwise, in air crashes. Close study of the large literature on air crashes indicates that impact of the body, especially the head, with some solid part of the aircraft is generally the cause of death or of serious injury, even in minor accidents. When the body or the head strikes something that yields, as when the flier is thrown through a fabric roof or the windshield, the victim generally escapes serious injury. What, then, are the basic factors that govern the degree of injury in such circumstances?

The most significant clues have come from two sources: De Haven's[32] analysis of nonfatal suicidal leaps from high buildings, and a study, for which Denny-Brown is largely responsible, of the effects of sudden acceleration on the head.

Nonfatal suicidal leaps. In a series of recent papers, De Haven[32, 33] has drawn attention to some remarkable cases of suicidal leaps from high buildings that proved not to be fatal. A number of such cases — in which all data were available concerning the exact distance of the fall, the position of the body during the fall and on landing, and the character of the surface that the body struck — permitted him to draw certain generalizations: in the nonfatal leap, the victim generally landed flat on the back or flat on the stomach, so that the long bones or the head was not driven into the trunk. But more interesting is the fact that a slight degree of cushioning of the head, as in landing in a garden plot instead of on a cement sidewalk, prevented concussion and serious injury of other parts. A typical case may be cited[33]:

A twenty-one-year-old woman, mentally depressed because of an amorous disappointment, took a room on the tenth floor of a hotel, consumed half a bottle of whiskey, and leapt in her nightdress to the street below — a free fall of 93 feet. She landed squarely on her back in a small garden in which the earth had been freshly turned, her head, back and legs sinking into the earth to a depth of 4 to 6 inches. A hand, which struck the cement border of the garden plot, suffered a fracture to a small bone in the wrist, but except for this and a fractured rib she was uninjured, suffered no concussion, and could walk without assistance. Her height was 5 feet, 7 inches, and her weight 115 pounds.

The important point about this and similar cases is that the head experienced a brief interval of deceleration, instead of an abrupt impact on a rigidly solid object. De Haven calculates that the girl's body was falling at a rate of 73 feet a second (50 miles an hour) at the time of the impact, and that the deceleration distance, which amounted to 4 to 6 inches of garden turf, must have taken place in a small fraction of a second; the rate of deceleration was 166 g (1 g = 32 feet per second per second). There is a vast difference between being decelerated from 50 miles an hour in 0.001 second and being decelerated in 0.1 or even in 0.01 second. Little attempt has been made so far to measure these brief but vital deceleratory time intervals in relation to injury.

A more complex case occurred several months ago in New York and is mentioned because of the relatively long distance of the fall. A woman leaped from the seventeenth floor, falling 144 feet, and landed in a "steamer-chair" position on a metal ventilator box 24 inches wide, 18 inches high and 10 feet long. The force of her fall, De Haven points out, crushed the structure to a depth of 12 to 18 inches. Both arms and one leg extended beyond the area of the ventilator, with resultant fractures of both bones of both forearms, the left humerus and the left os calcis. The woman remembered falling and landing, but had no marks

on her head or subsequent loss of consciousness. She sat up and asked to be taken back to her room. No evidence of abdominal or intrathoracic injury was found, and x-ray films failed to reveal other fractures. The minimum gravity increase in this case was 80 *g* (average, 100 *g*).

Stunt drivers. A practical application of the principle of gradual deceleration has long been used by circus performers and stunt drivers, who deliberately drive a car at 60 miles an hour into a brick wall. Their trade secret is to jump into the back seat of the car and lie hard against the rear of the front seat, a hand or an elbow being placed between the side of the head and the back of the front seat. The car then crashes into a solid object and the superstructure crumples up against the wall, but in a finite time interval sufficient to give adequate deceleration of the head and the rest of the body. If the head or the body were thrown without having the benefit of the car's own crumpling deceleration, "Reckless Peter," one of the best known of these stunt drivers, could be reckless no longer.

Aircraft[34] and automobiles, at the instigation of the National Safety Council, have been studied from the point of view of diminishing hazards to the head in the event of crash, and flying personnel are being indoctrinated with the principles of how to "take" crashes. For some pilots, this is instinctive, but the fact that the head and body should be placed hard against some solid part of the structure of the machine when a crash is anticipated is not commonly appreciated. Any yielding substance placed between the head and the solid area of superstructure has cushioning value in making deceleration more gradual; but if the head is free and hurled against the solid object at the time of a crash, the injury sustained is inevitably severer. Those stationed in the rear of the automobile or plane when it strikes a solid object have more opportunity for deceleration than personnel situated farther forward.

Experimental concussion. Denny-Brown and Russell[35] have approached the problem in the reverse direction,—namely, by analyzing factors of acceleration in relation to injury rather than through deceleration,—but the principles in the two approaches are the same. Denny-Brown and his collaborator have found that when the head of an animal is struck by a moving pendulum, concussion does not occur unless the head is free to move, free to be accelerated. If a head, hard against an anvil or a brick wall, is accidentally struck, a nasty fracture may result, but the subject is not rendered unconscious; for this an acceleration of the head in space is essential. In Denny-Brown's experiments, the rate of acceleration essential to cause concussion was relatively high: a critical value of 46,000 feet per second per second. If the head is cushioned, as by a helmet, the same blow may give the same ultimate velocity after the head has moved 5 mm., but if it does not start off with the same high acceleration, concussion is prevented. The implications of this in relation to crash helmets for absorbing blows from falling debris and flying bomb fragments are obvious, and it is no longer a secret that both the British and the Germans have a mandatory regulation to wear crash helmets in all operations of mechanized units, especially motorcycles. Such helmets have enormously diminished the number of serious head injuries sustained on being thrown, especially during blackout conditions.[36]

Ruptured intervertebral disks. A syndrome common in the military services, especially in air-force personnel, that is not often diagnosed is that of the ruptured intervertebral disk.[37] When men are maneuvering in aircraft, accelerations as great as 8 or 9 *g* may occur, that is, eight or nine times the normal acceleration of gravity, which cause strains on the vertebral column of intense character, making the weight of the torso at the lumbosacral articulation equal to about 800 pounds if the body weight of the pilot is 200 pounds. One means of lessening the physiological effects of high acceleration is the assumption of a crouched posture, which brings the lower extremities nearer the heart and thus diminishes the length of the hydrostatic column of blood subjected to accelerative force.[38] There is no doubt that the assumption of such a posture increases tolerance to high degrees of acceleration, but it also greatly increases strain on the lumbar vertebrae, the annulus fibrosus and the pulposus nuclei between the vertebrae. In these circumstances, one or more of the nuclei may rupture and herniate into the spinal canal, and thus may give rise to pain from compression of sensory-nerve trunks and rootlets. This accident, which is also common in civil life, especially in young adults, is one of the most frequent causes of acute and incapacitating sciatic pain.

The syndrome of the ruptured intervertebral disk is one with which every flight surgeon should be familiar, for the injury not only occurs as a result of high acceleration in aircraft but also is a common complication of injuries sustained as a result of a crash landing. Mild cases improve on simple immobilization, but there is a growing conviction among neurosurgeons, especially Spurling,[37] of Louisville, and Love,[39] of the Mayo Clinic, that when pain is enduring even with immobilization, operative removal of the ruptured disk is the only

satisfactory therapy. Group Captain Symonds,[40] of the Royal Air Force, reports on the British experience with ruptured disks and expresses his doubts of the wisdom of operation, for in his experience few, if any, cases can be returned to active service. Spurling,[41] on the other hand, reports that in his noncompensation group fully 75 per cent have returned to their former occupations within three months; the details of treatment must, however, be left to the neurologist and to the neurosurgeon.

From the point of view of aviation medicine, the importance of the intervertebral disk lies in the fact that one must be familiar with the condition so as to make positive diagnosis possible, and the flight surgeon should be interested in any procedure or device that will lessen the incidence of this accident in combat operations. Various forms of mechanical restraint, such as seat belts and shoulder harnesses, have been proposed to prevent flying personnel from being thrown or overstressed during landings and high-speed maneuvers, but there is as yet no unanimity of opinion on this point, and the matter is one that clearly deserves intensive study, not only for the purpose of diminishing lumbosacral injuries but also to reduce the large numbers of unnecessary injuries to the head sustained in combat maneuvers and crash landings.

Aftermath of Injury

The flight surgeon and other physicians who attend air-corps personnel not only must heed the problems of the air cadet in training or the pilot engaged in combat operation, but he must also consider the management of incapacitated flying personnel. Some may be wounded by machine-gun bullets, and others may be hurt less seriously by a crash landing or a violent air maneuver. Still others may deteriorate from fatigue, or from too many missions at a high altitude. A medical officer in charge of any command must be able quickly to distinguish the three types of incapacity and must know how best to manage each one — whether it is a physical injury from gunfire, an injury from crash or maneuver, or a psychological insult from anoxia.

Watson-Jones[42] in a recent stimulating paper, one of the few released for public consumption from the Royal Air Force, has discussed the ultimate problem with which all flight surgeons will sooner or later be faced, namely, the rehabilitation of personnel disabled by combat operation. He begins his article with a story of an injured air gunner.

> An air gunner was admitted to a civilian orthopaedic hospital in November 1940, for the treatment of a torn and displaced semilunar cartilage. In August 1941, no less than ten months after admission, he was still in hospital and still totally incapacitated. Why was recovery so long delayed? What possible explanation could there be? The diagnosis had been correctly made and a skilful operation performed. The wound had healed by first intention; there was no infection, arthritis, or surgical complication. Daily massage had been continued, but the muscles were still wasted and weak. Two manipulations had been performed under anaesthesia, but movement was only half of normal. The gait was slow and hesitant; he limped; he could not run — he had never tried to run. The medical officer blamed him because 'he would not co-operate,' because he was disinterested, depressed, and resentful. He was certainly depressed, for after ten months the incapacity was more complete than on the day of admission. He was disinterested because, in his own words, 'nobody takes any notice, and it looks as if it is hopeless.' He was resentful because he could not believe that the fault was his. Had he not been told that 'the nerve to his knee was cut'?
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> He was transferred to one of the orthopaedic rehabilitation centres of the R. A. F. Medical Service. He saw the sky, the sea, the open spaces. For many months he had seen only the stone walls of hospital wards, the stone walls of massage rooms, the stone walls of many corridors. In his new surroundings there was a lounge and writing-room; there were tasteful decorations and flowers, a varied menu, and an atmosphere of well-being and contentment. After a few days he smiled. There was sometimes a sparkle in his eye. He sensed a spirit of optimism and was reassured. His difficulties were explained, and he was taught special exercises. He learned to walk and then to run. He became an enthusiast and worked in the gymnasium, played on the fields, swam in the pool, cycled on the track. In the evenings he attended lectures and concerts, or played billiards and table-tennis. Time raced past, for he was busy. He became bronzed and fit. He laughed and was full of the joy of life. In seven weeks he returned to his unit and to full duty. The 'nerve in his knee' was forgotten.
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> Ten months — total incapacity; seven weeks — full recovery: that is the story of rehabilitation in one air gunner. But is this an isolated case from which no conclusion should be drawn?

We must face the fact that our air forces will bear the sting of heavy casualty; convalescent homes for study and rehabilitation of air-force personnel must be developed on a national scale, with a well-planned program for analysis of injuries peculiar to modern air combat, as well as facilities to meet the needs — physical and spiritual —of rehabilitation.

Watson-Jones's recommendations concerning the injured man in the air service are essentially conventional, at least conventional to our nonmilitary eyes in this country. But many military hospitals cannot study their cases from a scientific standpoint, and there may be many that would do for ten months what was done for the air gunner of Watson-Jones's report. It is highly important that the injured men from Pearl Harbor, Bataan, Corregidor, Cebu, Panay, Australia, Singapore,

Java, India, Africa, the Mediterranean and the North Atlantic sea lanes be given a sense of the importance of the contribution they have rendered, be given a sense of the part that they may still be able to contribute if put back into active service. I am not speaking as a psychiatrist, or even as a practical surgeon, but essentially as a layman. I have, however, had opportunity to survey the literature and have seen hospitals filled with sick men, seriously injured men, of the fighting forces of Britain; I cannot too vigorously emphasize the value of maintaining the morale of the injured man, of allowing him to take part in the care of others more seriously incapacitated than himself, and of giving him opportunity to discuss combat problems with those who have been placed before their injury in military situations similar to his own.

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Expansion of the air corps of both the United States Navy and Army has created an unprecedented need for medical personnel. The Navy within the year expects to complete training of more than 1000 air medical officers including several hundred flight surgeons, and Colonel David Grant, Air Surgeon of the Army, authorizes me to say that the Army Air Forces have now in service some 2300 medical officers and that an expansion is expected within the year to bring a total of 19,000 flight surgeons and aviation medical officers. If this demand is filled, it would alone absorb all the graduates of Class A medical schools in the United States during the past three years.

This war is probably more challenging to the physician than any other conflict in the world's history. Those who serve, especially those who serve the air forces, must have special knowledge; they must be cognizant of this, cognizant also of the part that they can play in maintaining air supremacy, and of re-establishing the right of free men to live in peace.

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VITAMIN B_1 AND ENDURANCE*

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RECENT reports[1] have indicated that the administration of vitamin B_1 may increase muscular endurance in subjects on a diet deficient in that vitamin. This effect is explained on the basis of the role of vitamin B_1 as an oxidative catalyst employed in the chemical process involved in muscular contraction. For this reason, men engaged in hard muscular work use more vitamin B_1 than those in sedentary occupations, and the amount suggested by investigators for workingmen and athletes is more than 300 international units daily. Yet Stiebeling and Phipard[2] report that a large number of people in the United States live on a diet poor in this vitamin.

The possibility of increasing human stamina and endurance, coupled with a fear of a probable lack of the vitamin, has been impressed on the public mind, and the use of synthetic vitamin B_1 has become widespread. It is employed not only in cases in which a definite vitamin deficiency has been found but also, in a more general way, as insurance against a possible lack of it. Tablets including thiamin chloride are supplied free in some industries; college athletes are given it, and even professional baseball players must take it to remain in the good graces of the management.

Recognizing the importance of vitamin B_1 and its strikingly beneficial effect in patients whose diet has been deficient in thiamin content, we questioned whether an excess of vitamin B_1 could increase the capacity of the human organism for work. At various colleges where either "shotgun prescriptions" including vitamin B_1 or this vitamin alone was being given to varsity athletes, no striking and convincing (at least for outsiders) results were obtained. At Springfield College, Coach Charles Silvia had been giving vitamin B complex, but no appreciable effect on the performance in swimming could be detected. The weakness in most of these "experiments" lies in the fact that they lacked controls. Usually, every member of the team received the same dose, and quantitative measures of performance were often impossible. How, for example, can one evaluate the effect of a certain vitamin on basketball players, football players and so forth? It is only when the amount of energy used can be measured, as in track running or swimming, that the tests become objective.

McCormick,[3] who attempted to improve endurance by giving his subjects a daily dose of 5 mg. of thiamin chloride in tablet form, used two tests: breath holding and arm holding. After one week of administration of vitamin B_1, he noticed definite improvement as measured by these tests. Since, in our judgment, McCormick's appraisal of the vitamin intake of his subjects was not convincing, and the results of the tests were not indicative of the vitamin effect, we decided to repeat his experiments.

Arm-holding test. Sixty-nine subjects, all of college age, were tested for the time they were able to hold their arms horizontally. For convenience, these men were divided into three groups (Table 1): in the first group, who were simply told to hold their arms outstretched as long as possible, the holding time ranged from 6 to 108 minutes; in the second group, who were given a "pep talk" with a reference to McCormick's record (which was erroneously announced as 135 minutes and was actually 145 minutes), the range of endurance varied from 8 to 135 minutes; in the third group, who were tested two days after the first two groups and, naturally, had been talking about the "remarkable" feat of holding the arms outstretched for 135 minutes, an especially emphatic "pep talk" was given and the range varied from 9 to 260 minutes.

TABLE 1. *Summary of Preliminary Arm-Holding Tests.*

ARM-HOLDING TIME	NO PEP TALK	PEP TALK	EMPHATIC PEP TALK
	NO. OF SUBJECTS	NO. OF SUBJECTS	NO. OF SUBJECTS
min.			
9 or less	8	5	1
10 to 29	7	14	15
30 to 119	2	2	6
120 to 190	–	2	6
260	–	–	1
Totals	17	23	29

Forty-one of the 50 men whose arm-holding times were less than 30 minutes were given either 5 mg. of thiamin hydrochloride a day or a placebo (5 mg. of lactose).§

A week later, the second test was given, the range varying from 5 to 77 minutes in the group who did not receive the vitamin, and from 7 to

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§The vitamin and placebo tablets were generously furnished by McKesson and Robbins, Incorporated, Bridgeport, Connecticut.

79 minutes in the men who did (Table 2). In the latter, 8 out of 16 improved, and in the former, 12 out of 25.

Of particular interest is the fact that some of the subjects who were given the preliminary test were on a high vitamin B_1 diet, and some were on a low diet. To the first group belonged the varsity swimmers, and to the second some of the wrestlers who were trying to lose weight. Of the 4 swimmers, 1 could not hold his arms out-

TABLE 2. *Summary of Arm-Holding Tests with and without Vitamin Therapy.*

Improvement over First Test	Vitamin Group	Control Group
%		
0–10	4	1
11–20	0	1
21–30	0	2
31–40	0	1
41–50	2	1
51–60	0	1
61–70	0	2
71–80	1	1
81–90	0	1
91–100	1	0
101–200	3	2
201–300	2	6
301–400	0	2
401–500	2	1
501 or more	1	1
Decrease in ability	0	2
Totals	16	25

stretched for more than 10 minutes, and 2 of the others, for more than 60 minutes. Of the 2 wrestlers, one held the position for 161 minutes, and the other for 260 minutes (4 hours and 20 minutes).

These tests showed either that all the men had a sufficient amount of vitamin B_1, which was questionable in the wrestlers, or that arm holding cannot be used as a test for the effect of the vitamin in apparently normal people, or for vitamin B_1 at all, because the test is definitely affected by psychologic factors, such as a "pep talk" and the competitive elements involved.

The arm-holding test has been used by other investigators[4, 5] to detect the changes in endurance due to various modifications of the diet. In view of the evidence here presented, the reliability of this test as an indication of muscular endurance should be seriously questioned. Persons who are easily affected by suggestion, or even by autosuggestion, are apt to give a better performance in this test.

The breath-holding test. This is one of the routine class tests given at Springfield College in a course of instruction in the physiology of exercise. During hundreds of tests, it has been observed that the psychologic factors greatly influence the time of breath holding. Nevertheless, we used a group of 20 men for this experiment. They were given two breath-holding tests in succession, and then half the subjects were put on a diet containing 5 mg. of thiamin chloride a day for a week, and half on one containing 5 mg. of lactose a day. No effect of vitamin B_1 on breath-holding ability was observed.

Conclusions

Vitamin B_1 deficiency in apparently normal college students cannot be discovered by means of either the arm-holding or the breath-holding test.

These tests may be greatly affected by psychologic factors, and are therefore not reliable indications of the degree of muscular endurance.

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KELOIDS AND THEIR TREATMENT*

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KELOIDS may be defined as an exaggerated growth of scar tissue. In this exaggeration, they appear to defy to some extent the normal rules of growth, and have accordingly been considered a bridge or link between normal reparative processes and actual neoplastic changes. However, unlike neoplastic growths, the keloid process is initiated from normal fibroblastic cells solely by trauma. These cells produce the keloid by carrying on their normal function — although to an exaggerated degree. This exaggeration continues even after excision, and in fact, the tendency to recur is the most characteristic feature of the growths. Were this not so, keloids would cease to be a problem.

In their growth, keloids become thicker and heavier and actually extend out into adjacent normal skin, well beyond the border of the original injury. This quality of extending beyond the site of the original injury is a pathognomonic feature of keloids and helps differentiate them from hypertrophic heaped-up scars or cicatrices, which develop at the site of suppuration or the site of previous loss of tissue, are limited entirely to the areas involved by suppuration or trauma, and gradually shrink and become less conspicuous. Keloids always project above the level of the surrounding skin, but extend very little, if at all, into the underlying subcutaneous tissue. In fact, in secondary abdominal operations involving the excision of a keloid occurring in a previous incision, relatively little scar tissue may be encountered in the subcutaneous fat, although the skin keloid may be very heavy.

ETIOLOGIC FACTORS

Trauma is always the precipitating etiologic factor in the production of keloids. Keloids probably never occur without the preliminary destruction of cells by some form of physical or chemical violence. However, only certain persons consistently develop keloids after moderate trauma. This tendency indicates some sort of fibroblastic diathesis, varying in intensity among races and individuals. Furthermore, the sensitivity of the fibroblasts to substances provoking proliferation and growth may change as the patient gets older and as the rate of growth and metabolism alters. This accounts for the relative scarcity of keloids beyond the age of fifty. Indeed, it is very rare in the aged, whereas it is rather frequent in the young. In a survey of 50 cases of appendectomy for chronic appendicitis in children between the ages of five and fifteen years, various degrees of keloids were noted in 28 cases — a high percentage.

There are also local influencing factors. Keloids occur only rarely on the face, forehead, hands and feet, front of the neck, axilla, inguinal region, anal region and perineum, whereas they are common around the ears, sides and back of the neck, abdomen and chest (particularly in women). Keloids seldom, if ever, occur in incisions placed in natural flexion creases, although they may occur in incisions or scars running across flexion creases. The only explanation for this phenomenon seems to be the manner in which tension is applied to different areas in the body. It will be noted that in those regions in which keloids seldom occur, the skin and underlying tissues are subject to constantly changing degrees of tension and stress. These areas are very often moved and shifted in the course of ordinary activity. There is a considerable amount of constantly changing stress and strain in the flexion creases and in the perianal and perineal regions. On the contrary, where keloids occur frequently, the skin is under the normal degree of tension but remains almost constantly so with relatively little motion and change. In areas where there is no skin tension whatever,— as in the scrotum and in the upper eyelids,— keloids do not occur. One other interesting phenomenon is the rarity of keloids in the hairy regions of the body. All these local factors are of primary importance in the selection of sites for incisions and in the prevention and treatment of keloids.

TREATMENT

The treatments advocated for keloids have been legion. If one is shocked at the lack of rationale of some of them, one may at least admire their ingenuity. Lesieur[1] injected oil of creosote, and Smyth[2] used formalin. Attempts at digestion of the keloid were made by Ahlswede,[3] who used a mixture of pepsin and hydrochloric acid. Hoffman,[4] in his paper advocating radiation as the treatment of choice, lists twelve methods of treatment collected from the literature, but many more can be gathered without difficulty. These vary

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from Sheehan's[5] "capillary" drainage to iodine ionization, advocated by Grain.[6] Cannon[7] painted the lesions with trichloracetic acid to thin out the keratotic layers and then subjected the lesions to roentgen radiation. This author also recommends desiccation, preceded and followed by x-ray treatment. Unna[8] reported a patient cured of a keloid by the application of pressure renewed weekly for three months.

No one treatment produces good results in all keloids, but considerable success may be attained consistently if all factors in each case are carefully considered. A keloid in a given patient is not a stereotyped condition. The very realization that one is dealing with a lesion that occurs because of a specific type of diathesis and may be influenced by local factors will in itself serve to orient one in the consideration of the proper treatment. Certain essential principles must be adhered to. These are the avoidance of further trauma, the release of constant excessive tension, the application of pressure, and the careful use of surgery in addition to radiation.

Rough handling, vigorous massage, careless surgery and the application of traction serve to aggravate or reproduce the keloid. Whatever procedure is carried out, it is well to remember that trauma produced the lesion to begin with, and that by no stretch of the imagination can one believe that trauma can also effect a cure. Nowhere in the realm of surgery does a satisfactory end result depend so much on scrupulous, atraumatic technic as in the surgical removal of keloids. The use of a sharp knife, fine-pointed forceps and sharp, cutting-edge, atraumatic needles is necessary. The exact type of suture material or stitch does not matter. Subcuticular sutures are apt to give poorer approximation and more reaction than the more orthodox ones. The suture material should be as fine as possible — preferably a No. 000000 dermal plastic suture. A cutting-edge needle is far less traumatizing than a round needle. If the wound is not under tension, the sutures should be removed in forty-eight to seventy-two hours. Very accurate approximation, of course, needs no further emphasis.

Constant excessive tension must be released either as a preliminary to further surgery or radiation or in the process of excision. If a keloid is excised and the edges approximated under exactly the same conditions of tension as previously existed, the keloid will certainly recur. It is for this reason that simple excision is inadequate. The essential fact is that the direction of established stresses should be changed if possible. A Z plastic is of invaluable aid in such a situation (Fig. 1). This produces a rotation of the vertical portion of the Z to the horizontal, and rotates the direction of the maximum tissue tension 90°. Simple excision may be carried out successfully on the abdomen, the upper extremity and the neck.

Subsequent tension may be avoided by judicious choice of flap plastics in place of free skin grafts. Free grafts of all sorts tend to contract and pull the surrounding tissues around them. When a pedicle graft may be used in place of simple suture of skin graft, it is preferable. Releasing incisions are very useful provided they do not jeopardize the cosmetic result. If they can be placed in a natural crease or within a hairline, they serve as a valuable adjunct. Satisfactory results may be obtained in the excision of a keloid from the back of the neck by the use of a parallel releasing incision placed 3 or 4 cm. higher up in the scalp itself. The combination of the releasing incision and the flap is illustrated by a type of plastic very

FIGURE 1. *The Z Plastic.*

A — the keloid has been excised, and two parallel incisions made, defining two flaps (a and b); B — the flaps are transposed and sutured; note that the lines of tension are rotated through 90°.

suitable for keloids over the broad surfaces of the body, such as the chest and back (Fig. 2). This consists of excision of the keloid and then the making of a V-shaped incision a suitable distance from the defect so that a flap may be raised and transplanted to obliterate the original defect. The V-shaped defect in the new incision is then closed in a Y-shaped approximation.

The use of radiation for the treatment or prevention of recurrences of keloids is by no means so logical or consistently successful as some reports indicate. The old, well-developed keloids are extremely resistant; the younger ones respond well to radiation. Hence, if radiation is to be employed, well-developed keloids should first be excised, so that they may be supplanted by a young keloid. The best results reported are in those series in which radiation, from three to five days postoperatively, is given after surgical excision. It is assumed that at that time the young proliferating fibroblasts are most sensitive to radiation. In fact, radiation delayed a few days after excision yields better results than radiation given into the open wound at the time of or within twenty-four hours of operation.

Excision of the keloid, in addition to any plastic procedure necessary to relieve tension, followed by radiation in moderate dosage from three to five days postoperatively is what I believe to be the method of choice in most cases.

The use of pressure, when applicable, may yield excellent results with no risk of recurrence. It is not rare to note keloid formation in the lower half of a low abdominal scar, whereas in the upper portion — where the imprint of the elastic of an undergarment or belt may be seen — no keloid is present. The ischemia produced by the pressure arrests overproduction of scar tissue. Slight but constant pressure may be applied to some portions of the body over long periods. Over the extremities, the abdomen and the shoulders, pressure by means of adhesive strapping may be utilized with comfort. The simplest method is to fashion a throat stick, a piece of dental impression compound or a piece of heavy felt to conform to the shape of the keloid. This mold is then strapped tightly to the keloid. Strappings should be changed weekly. If adequate pressure is applied, a remarkable change is noted after the first week, but if the pressure is not continued, the keloid quickly resumes its original prominence. The strapping, therefore, should be renewed weekly, with no interruption for at least six to eight weeks, and possibly longer. This method is particularly applicable to young keloids, which are more vascular and contain less collagenous material than the old ones. The local anemia induced by the pressure has more effect on the more vascular lesions. Obviously, pressure is not applicable to the face, the neck, the front of the chest and parts of the back. Pressure may be utilized in the prevention of recurrences by the simple expedient of keeping the incision covered with a strip of adhesive plaster for many weeks. The light, even pressure of the adhesive results in a much smoother, softer scar, with practically no elevation above the skin.

If keloids recur, the average time of recurrence is two or three weeks. Evidence of return may even be noted within two weeks. However, if keloids do not recur within six to eight weeks, one may consider subsequent recurrence extremely remote.

FIGURE 2. *The V-Y Plastic.*

A — the keloid has been excised, and a V-shaped incision made, parallel to the long axis; B — the original defect is closed in a straight line, and the V-shaped defect as a Y; such closure produces no tension.

RESULTS

The following results were obtained from observations on fifty-one keloids in 49 patients. The cases were grouped according to the method of treatment, as follows: excision and reapproximation; radiation; excision and radiation; and pressure. Table 1 indicates the results obtained. For the purposes of tabulation, a result was considered satisfactory when the keloid was not longer present, or when it was strikingly improved. A fair

result was indicated by definite, but partial, improvement, and an unsatisfactory result by a case in which the keloid remained unchanged, recurred or became more marked.

Summary and Conclusions

The exact etiologic factors in the production of keloids are not known, but there is sufficient evidence to indicate wide variations in racial and individual susceptibility. In addition, certain local factors, particularly the manner in which local skin tension is applied, may be shown to have a determining influence in the occurrence of keloids. Areas in which skin tension is constant are apter to be the site of keloids, whereas in areas where there are frequent changes in tension of the skin, — such as the creases, — keloids rarely occur. In these areas, keloids do occur if the original scar is sufficiently extensive or if it extends across the normal lines of tension.

Treatment consists in the avoidance of further trauma, the release of constant and excessive tension, the careful use of surgery, in addition to radiation, and, rarely, the use of pressure alone. Pressure may also be employed to prevent recurrence after excision. When pressure cannot be utilized, the treatment of choice consists in excision of the keloid, in addition to any plastic procedure necessary to relieve tension, followed by radiation in moderate dosage beginning from three to five days postoperatively.

Table 1. *Results of Four Methods of Treatment.*

Treatment	No. of Cases	Result		
		Satisfactory	Fair	Unsatisfactory
Simple excision and reapproximation...	12	2	2	8
Radiation	9	4	1	4
Excision and radiation (3 to 5 days).....	19	10	6	3
Pressure	11	7	2	2
Totals	51	23	11	17

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MEDICAL PROGRESS

OTOLOGY: THE TREATMENT OF DEAFNESS IN THE LIGHT OF RECENT ANIMAL EXPERIMENTATION*

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To treat the deaf successfully has been the ambition of all otolaryngologists. Unfortunately, the otologist is immediately on the defensive when the patient announces that he is deaf. The mental sigh of relief when large plugs of cerumen are found is almost audible, for here is something to be done that will give relief. As for the other types of deafness, except for certain conditions such as the acute suppurative and the secretory ear, the otologist, after establishing the diagnosis, considers the case hopeless and subconsciously prays that the patient will not return. This defeatist point of view is not due to lack of knowledge of methods of treatment used at present, but to a failure to realize that many types of deafness can be helped even though the condition cannot be cured. To approach this subject intelligently, one must have an understanding of the present conception of how people hear.

Hearing is not a function of the middle or inner ear alone but is in reality a phenomenon of the brain resulting from the interpretation of nerve impulses coming to it from the sense organ for hearing, the organ of Corti. The basic requirements for hearing are a normal sense organ to receive the sound waves and a normal brain to interpret the messages received from the sense organ. The middle ear and its structures are aids and refinements for acute hearing but are not essential to hearing, for which other apparatus can be substituted in certain types of deafness.

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The statement that a normal brain is essential for hearing may raise doubts in many minds, but I should like to point out that all animals of the mammalian group (man is one) hear in the same manner but that the interpretation of the sense-organ stimulation varies tremendously with the development of the brain. The newborn infant does not hear until he has learned to interpret the stimuli received, and as the interpretative power of the child increases so does his hearing, for it is from this ability to interpret and repeat the sounds heard that speech and its accessories, reading and writing, have developed.

The membranous labyrinth, with its vestibular and cochlear sense organs, is well known and requires no detailed description. I should like to draw attention to the way these two sense organs work. They both depend on movements of fluid to stimulate them. The vestibular apparatus requires movement of the endolymph — that is, movement of the fluid inside the membranous vestibular structures. The cochlear mechanism depends on movement of the perilymph, which is outside the membranous cochlea. Thus, the vestibular portion can be called the endolymphatic system of the membranous labyrinth. The cochlear portion can be called the perilymphatic system of the membranous labyrinth. This distinction is important and is more fuliy discussed below.

The organ of Corti is the sense organ for hearing. It consists of specialized neuroepithelial hair cells, which are probably stimulated by movement of the basilar membrane. The membranous cochlea is so arranged that the stimulation is through the perilymph, as one can easily see when examining the relation of the membranous cochlea (scala media) to the perilymphatic spaces, the scala vestibuli and tympani. The organ of Corti is not concerned in the question of how this movement of the perilymph is obtained, but once it is produced in sufficient strength to cause movement, it responds and the resulting sensation is hearing.

Thus, deafness divides itself into two types. The first is that in which the organ of Corti itself is involved: the hair cells may degenerate, and as a result, there is an inability of the organ of Corti to respond to the fluid-pressure changes, even though these pressures are made in a normal manner. This lack of response has been called "nerve deafness," because it was thought to be a degeneration of the cochlear nerve; "variable deafness," because there are a great many types of hearing loss with this condition; and "perception deafness," because the deafness is a result of failure of the sense organ to respond to the stimuli sent to it. These three terms indicate the same type of deafness. In the second type, the fluid-pressure changes are prevented, or made more difficult to produce, in the perilymph. The organ of Corti is normal, but with lack of stimulation, there is no response. This type of deafness, which is due to the inability of the external air-pressure changes or air sound waves to be transmitted to the perilymph, is therefore called "transmission deafness" or "middle-ear deafness," for these structures are involved.

The middle ear and its structures have to do with the changing of air-wave pressures into fluid-wave pressures. Anything interfering with this function results in a loss of hearing. The plugging of the external ear by wax or debris is the simplest type to remedy. Pathologic conditions of the middle-ear structures, such as fusion of the malleus and incus or adhesions around the ossicles, which prevent them from moving freely, the thickened and retracted drum, perforations of the drum, chronic suppuration and acute suppuration of the middle ear, all cause deafness for air-borne sounds, for they interfere with their transmission. Otosclerosis acts in a similar manner, that is, by an interference with air-borne sounds. Sound waves transmitted by the vibration of the bone structures surrounding the membranous cochlea are not interfered with, and the normal organ of Corti responds readily to them.

Thus, it is the duty of the otologist to use all the knowledge he has to overcome this transmission difficulty. Mechanical means, such as the hearing trumpet and the fan that is held by the teeth, to conduct sound waves to the cochlea have been employed. The new hearing aids are of great benefit to many. Most of these patients can be helped if the otologist will take time and effort to find the method to be used. A great many patients with large posterior perforations are helped by the application of a paper drum, which can be made out of patipar paper, is waterproof and stays in place very readily. One can be pleasantly surprised at the amount of hearing improvement obtained by the use of a paper drum. The making of absorbent-cotton drums should be known to all, and many patients have used them for years.

One of the finest appliances for patients with a posterior perforation or absence of the drum or ossicles, and even in those who have had radical mastoid operations, is the Pohlman[1] apparatus. This device has proved very satisfactory, even in cases that are discharging and in dry cavities. The principle on which it is based is the replacing of the former normal human transmitting apparatus with one similar to the bird's middle ear. This appliance, when in place, can be worn for long periods. Patients have had them in as

long as eight or nine months and have heard remarkably well with them.

All the methods described above depend for their good results on the ability of the apparatus used to change the air-borne sounds into fluid waves, and a normal or almost normal organ of Corti to respond to the stimulation. It would be unwise to expect these aids to enable a patient with a diseased or degenerated organ of Corti to hear better, for no matter how good the transmission, there is no sense organ to respond.

Thus, the fenestration operations of Holmgren, Sourdille and Lempert are sound from this point of view, and they should work so long as the perilymph can be stimulated by air-pressure changes, that is, by sound waves. It must be perilymph stimulation and not endolymph stimulation. Stimulation from endolymph-pressure changes results in vestibular responses such as dizziness and nystagmus. The fact that a case of fistulization responds to pressure changes of the endolymph is not necessarily an indication that the perilymph is also responding to air-pressure changes. The difficulty with the fenestration operation is not that it will not work, but in keeping the fistula in such a state that the perilymph will continue to respond to sound waves. New-bone formation, fibrous bands and even a complete blocking of the perilymphatic spaces around the fistula will nullify all the efforts of the operation. The fistula operation is a definite step forward in the attempt to cure transmission deafness. Whether such deafness is due to otosclerosis or middle-ear deafness is immaterial. The main question to be kept in mind with this operation is, Has the patient a normal or nearly normal organ of Corti to respond to the resulting stimulation? If not, the operation should not be done.

The present technical difficulties will be overcome in the near future. Only time will tell if the regeneration of bone or the other mishaps that have occurred in this operation can be prevented. Thus, it does not behoove one to take sides regarding this operation, but to allow time and further experimentation to tell the story. Again, one must remember that the new technics are not easily acquired. No otologist at the present time should expect to get results in his early operations. In fact, it should be emphasized that it is an operation for the younger generation of otologists to attempt and then only after an arduous and thorough training in its technics and indications. There is no doubt that the fenestration operation will have a definite place in the otology of the future.

Middle-ear or transmission deafness, except otosclerosis, results from neglect of mild middle-ear disease caused by the common cold, with its blocked eustachian tube. There is a great deal of literature on this subject, but many otologists still do not realize that it is their duty to warn the public and to emphasize the fact that a great deal of middle-ear deafness can be prevented. The children with the neglected mild catarrhal or secretory ears are the future middle-ear deaf persons of adult life.

Middle-ear deafness is a problem that has been attacked in a great many ways, for its chief fundamental pathology is the prevention of sound waves reaching the organ of Corti, and this can be overcome. The great challenge to the otologist is nerve deafness of the acquired or inherited type. Before undertaking the treatment of this disorder, one must understand it. Is it nerve degeneration or degeneration of the sense organ itself? Nerve deafness can theoretically occur in one of three ways: by destruction of the central nerve pathways for auditory stimuli, such as hemorrhage in the brain, intracranial tumors and arteriosclerosis with degeneration of the auditory cortex; by degeneration of the cochlear nerve secondary to meningitis, as in cerebrospinal meningitis, influenzal meningitis, syphilis, acoustic neuromas in the external auditory meatus and toxic conditions that may attack the nerve endings; and by degeneration of the sense organ itself — that is, degeneration of the internal and external hair cells, accompanied by secondary degeneration of the cochlear nerve.

In nerve deafness, one characteristic stands out. The patient can hear the sounds but cannot make the words out accurately. He is always complaining that people do not articulate properly. They mumble, and as a result he cannot hear. What does he miss? He misses the very fine, high sounds of small intensity. These high-frequency sounds make the difference between words that have similar vowels but different consonants. If the intensity of the spoken words is increased, the patient has less difficulty in distinguishing them. He has trouble hearing people on the telephone and can never hear everyone at the dinner table or in a room filled with people talking at the same time. Noisy places bother him. He hears best when conversing with a single person.

There is no evidence from these people that their brains cannot interpret, but there is an indication that the auditory impulses received by the brain from the organ of Corti are the result of sound waves not received accurately. If the cochlear nerve is at fault, one would expect complete blocking off of the impulses from the organ of Corti, with a resulting complete loss of hearing for the area involved. This does happen in some cases, with complete loss of tones above 5000 but with normal responses below these frequencies. Others may have definite islands of deafness. But the majority of nerve-deaf people hear all tones from 64 to 8000 cycles per second when they are made

loud enough; this shows that the nerve itself is not primarily responsible for this type of deafness.

From experimental studies on animals and human beings, the evidence at present is that the end organ itself is primarily the cause of nerve or perception deafness.[2, 3] The following data were obtained from animals, for it is from this material that the treatment of nerve deafness can be evaluated.

It has been known for years that people exposed to loud sounds for long periods become deaf, and the type of deafness that develops is a nerve deafness. It has been called blacksmiths' deafness, boilermakers' deafness, riveters' deafness and, recently, aviators' deafness. Animal experimentation definitely shows that this type of deafness is the result of degeneration of the organ of Corti; the external hair cells go first, and then the internal hair cells. The testing of the electrical response of the organ of Corti of experimental animals showed a typical loss of function similar to that of the nerve-deaf person. This was confirmed by the fact that the person subjecting these animals to the sounds also lost his hearing in a similar manner. Exposure of human subjects to extremely loud sounds for short periods gave similar results. Fortunately, the human organ of Corti recovered from these experimental exposures, but there is no question that if the exposures were repeated more frequently and for longer periods, there would be a marked and permanent loss of hearing owing to degeneration of the hair cells.[2, 3]

Chemical poisoning of guinea pigs in which prolonged doses of quinine were given also resulted in degeneration of the hair cells. Animals were found that were deaf secondary to disease of unknown origin. They also had degeneration of the external hair cells, and some degeneration of the internal hair cells. In the last group of animals (deaf as result of disease), there was also degeneration of the cochlear nerve. In the first two groups, the cochlear nerve gave no evidence of gross degeneration.[3]

This experimental work demonstrates that the nerve-deaf person has a degeneration of the external hair cells scattered over a large area of the organ of Corti. As a result, he has lost his ability to interpret the fine and weak sounds of high frequency, and this loss causes his deafness. If the sounds are made louder, his interpretation is better, because internal hairs begin to respond to the stimuli and the hearing is improved.[3]

The nerve-deaf person first appears for treatment when he has already lost between 20 and 40 decibels of hearing. The reason is that the deafness comes on gradually and over a long period. It may be years before he notices that he no longer can hear as other people do. To treat this patient with the expectation of restoring hearing is futile. To treat with the expectation or hope of preventing further loss or even slight improvement is justifiable.

A number of factors causing degeneration of the hair cells may be grouped as follows: toxic poisons such as alcohol to excess, tobacco, quinine and salicylic acid compounds; chronic infections, with toxic absorption affecting the end-organ apparatus; endocrine disturbances; and certain diseases, such as pneumonia, influenza, mumps, syphilis and meningitis, attacking either the nerve or the organ of Corti. Any one or all in various combinations can cause nerve deafness.

One must remember, in treating these patients, that no cure can be promised or expected. In the majority of cases, nothing can be done except to try to prevent further damage to the organ of Corti. Degenerated hair cells cannot be restored. All one can do is to try to prevent further degeneration, and even this may be impossible. It is true that every now and then one seems to improve the hearing in some of the nerve-deaf people. This is usually the result of improving the general health of the patient or of treating the endocrine defect if it can be found. In all cases, one should build up the general physical condition of the patient. Vitamins or estrogenic substances, it must be understood, are not cures for deafness. They cannot restore degenerated or absorbed hair cells and nerve-ganglia cells that are gone.

Tinnitus that is possibly due to nerve irritation may be temporarily relieved by the use of the vitamin B complex in large doses. Selfridge[4] and others have reported their results. The experimental work with vitamins, as reported by Mellanby[5] and Covell,[6, 7] was done on very young and rapidly growing animals. The experiments performed on adult animals have not, as yet, produced the same results. It is not rational to expect that vitamins will restore to normal function a sense organ that for years has been degenerating because of disease or lack of vitamins. The majority of people with this complaint are over thirty years of age.

A great many of the nerve-deaf patients also have middle-ear conditions that can be helped, and it is in the treatment of such conditions that the best results have been obtained, not in the actual restoring of the organ of Corti, but in the improvement of the mechanism that has to do with transmission of sound, so that the patient can use his sense organ to its greatest efficiency.

Thyroid has also been used as a cure for deafness. The only cases I have found that were helped were definite hypothyroid cases in which the loss of hearing was due to the slow cerebration of

the patient rather than to a true loss of sense-organ cells.

There is also a group of patients that inherit deafness, not the congenitally deaf, but persons who begin to lose hearing at definite ages, from puberty to forty-five years; their histories indicate that members of their families have sustained the same loss. Nothing can be done for them. It is interesting that animals also have this tendency to inherit deafness. In these animals, the deafness is primarily due to a degeneration of the hair cells of the organ of Corti.[8] Otosclerosis is considered an inherited disease in which there is first a middle-ear and later a nerve deafness.

In recent experimental work on human beings, it has been demonstrated that tinnitus of definite pitch is due to irritation of the organ of Corti itself. The pitch of the tinnitus could be determined on either side of the traumatic lesion caused. Further proof of the organ of Corti as the cause of tinnitus with definite pitch was found in experiments on human beings in which the cochlea was stimulated electrically.[9] It was impossible to stimulate the cochlear nerve and obtain definite pitch. The sound reported on stimulation of the cochlear nerve was a general buzzing or hissing noise, but no accurate placing of pitch was possible. That the nerve was being stimulated was proved by the fact that there was also response of the vestibular nerve, which was being stimulated at the same time.

In a number of cases, in which the hearing loss was due to labyrinthitis, one could not get responses for tones except where the organ of Corti was present and definite tone islands were found. Patients with middle-ear deafness due to large perforations, ossiculectomy or radical mastoid operations responded to tones up and down the range very accurately, and could match the tone with air-borne sounds sent to the other ear. These experiments on human subjects have definitely shown that stimulation of the nerve itself cannot enable the patient to hear. The sense organ must be present.

In studies being done on traumatic deafness, it has been possible to demonstrate trauma to the organ of Corti. In one of these experiments, it took several days for the subject's hearing to come back to normal. Studies on animals showed similar results and indicate that disorganization of the hair cells and not the nerve is the primary cause of traumatic deafness.[2, 3]

One must view with a great deal of caution all claims for curing deafness that depend on systemic treatment. I know of no drugs or methods of treatment that will restore hair cells once they have degenerated. Again, prevention and not attempt at cure is the only hope.

The organ of Corti is the last of the special senses to be developed. It is a most sensitive sense organ, and is easily affected by a great many factors, such as disease, chemical poisons and trauma. No other sense organ in the body reacts so quickly to physical disturbances. In fact, in some ways, the cochlea is an indication not only of physical well-being but also of actual age in its relation to the body structures. Thus, at the present time, methods of treating the nerve-deaf person are limited to the removal of poisons, either chemical or toxic, and to the improvement of the general health of the patient.

* * *

It should be emphasized that one can and should do more to help the patients with middle-ear deafness. It takes time, and progress may be slow, but with hearing appliances and with the future possibilities of the fenestration operation one should be more willing to undertake the treatment of these cases.

In nerve deafness, the general physical well-being of the patient should be raised to as high a level as possible. Vitamins and other drugs that are necessary to bring about this condition should be used. Foci of infection causing toxic absorption should be removed. Toxic substances, such as tobacco, alcohol and drugs, should be completely eliminated; partial discontinuance is of no benefit. The results will not be cures, but in all probability, healthier persons who will be able to use to the utmost the hearing that is left.

In many ways, man by his inventions has caused a great deal of deafness. Nature makes few noises that are capable of causing deafness. Man has made many, such as airplanes, riveting machines, explosives, tanks and machinery. One must appeal to the acoustical engineer to reduce, so far as possible, the man-made noises that are causing this delicate and very sensitive apparatus of hearing, the organ of Corti, to degenerate.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28221

PRESENTATION OF CASE

A fifty-eight-year-old housewife was admitted to the hospital because of abdominal pain.

In the seven weeks preceding entry, the patient had three episodes of pain and distress in the right upper abdomen associated with nausea and vomiting. Each attack came on rapidly at about three o'clock in the morning following a meal that included "rich foods." Each attack lasted about a day and left the patient feeling very weak. The pain was not cramping and did not radiate. There were no chills, fever or jaundice. The vomitus was never bloody or like coffee grounds. Fourteen hours before entry, the patient was awakened by severe, steady pain in the right upper abdomen and epigastrium. She felt nauseated, and vomited. There was much abdominal distention, some of which was relieved by the passage of gas by rectum. The abdominal pain continued unabated, and at the time of entry there was some pain in the right shoulder. On the morning of entry, the patient had a chill. The bowel movement on the day before the attack was "darker" than usual, although not bloody or tarry. The patient was usually constipated.

Twenty-five years before entry, she had an appendectomy. Twelve years later, she had several attacks of fainting and coughing, with slight hematemesis. A physician took roentgenograms and told the patient that she had "ulcers." She went on a Sippy diet and had no further complaints except for intolerance to fatty foods.

On admission, the patient appeared ill and pale. The heart was within upper limits of normal size. The lungs seemed clear. Deep respiration was painful. The abdomen was slightly distended, without apparent peristalsis. There was tenderness without spasm throughout the abdomen centering in the right upper quadrant. No masses were palpable.

The blood pressure was 122 systolic, 60 diastolic. The temperature was 99.5°F., the pulse 80, and the respirations 18.

Examination of the blood showed a white-cell count of 19,600. The blood Hinton reaction was negative. The urine was normal.

On the first hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. SWEET: Attacks of pain such as this patient had coming on at three o'clock in the morning after an evening meal of rich foods are likely to be caused by gallstones.

The temperature of 99.5°F., the pulse of 80 and the respiratory rate of 18 seem inconsistent with the statement that "the patient appeared ill and pale." At any rate, there was no shock.

From the past history, one can say with reasonable certainty that the patient had gallstones. On the other hand, a predominating factor in all the attacks was nausea and vomiting. In uncomplicated cholelithiasis, that is not common. When nausea and vomiting occur, one should suspect some complication of stones, such as cholecystitis or pancreatitis. The late Dr. Daniel F. Jones used to say that patients with gallstones rarely vomit. In spite of this, I shall assume from the past history that the patient did have gallstones.

I should like to exclude ulcer in this case in spite of the fact that an x-ray diagnosis of ulcer was made thirteen years before entry. There is very little to suggest ulcer to me unless we were dealing with an acute perforation. It is reasonable to assume that there was no acute perforation because the patient was apparently not sick enough. There was tenderness, but no spasm. Widespread tenderness without spasm is certainly not consistent with peritonitis.

I assume that she had gallstones with some complication. One must bring out certain points about the history to decide what the complication might have been. It is impressive that the pain was steady and very severe, and yet the patient was not very ill, according to the record. Could she therefore have had acute cholecystitis? The majority of patients with acute cholecystitis in my experience are apt to have rather higher temperatures when we first see them and often have higher white-cell counts: 19,600 is a high count, but acute cholecystitis is often associated with a count of 30,000 or more. The patient may have had acute cholecystitis, but I doubt it.

What else might she have had? Acute pancreatitis must be considered, especially as a complication in cases of gallstones. Acute pancreatitis alone would not explain the repeated attacks for a period of three months, but she might have had stones and then a final attack of pancreatitis. At any rate, the steady pain, the excessive nausea and vomiting, the pain in the shoulder on deep inspiration, the elevated white-cell count and the chill, which occurred not at the onset of symptoms but some time afterward, suggest it.

In this particular case, it is a difficult matter to differentiate cholecystitis and acute pancreatitis

complicating gallstones. If we take the physical examination as it reads, I presume that we must exclude pancreatitis because no mention is made of tenderness in the left upper quadrant; it is all in the right upper quadrant. The pain in the shoulder was also on the right side. However, I should not be at all surprised if she did have acute pancreatitis for the reasons that I have mentioned. It is because of nothing more than the clinical picture that I should lay more emphasis on pancreatitis than on acute cholecystitis. An observation that would have been of great value in differentiating such a case seen early after the onset would have been a serum or urinary amylase determination, or both. In early cases of acute pancreatitis, it has been helpful in some patients. I am reasonably certain that the surgeon who operated on this patient did not believe it was pancreatitis. We have learned, of late years, the disadvantages of early operation in cases of this sort, but I should not be at all surprised if that is what she had in addition to gallstones. I do not believe she had cholecystitis.

Clinical Diagnosis

Peritonitis, probably due to perforated gall bladder.

Dr. Sweet's Diagnoses

Cholelithiasis.
Acute pancreatitis.

Anatomical Diagnoses

Foreign-body perforation of ileum.
General peritonitis.

Pathological Discussion

Dr. Tracy B. Mallory: I am afraid that the description of the abdominal findings as given in the abstract must be very inadequate, since the preoperative diagnosis was rupture of the gall bladder and general peritonitis. I shall ask Dr. Allen to take up the story.

Dr. Arthur W. Allen: The patient had had repeated attacks of acute abdominal pain for several months, and her physician was so convinced that these were attacks of gallstone colic that he had had two Graham tests performed outside. The clinical story was not too convincing, but we believed that the acute episode was probably associated with the gall bladder. We thought of acute perforation because there was too much generalized spasm and tenderness in the abdomen to be accounted for on the basis of simple acute cholecystitis, and we operated under the diagnosis of perforated gall bladder with peritonitis. At operation, it was obvious that the gall bladder and everything in the upper gastrointestinal tract were normal — no perforation of an ulcer or of the gall bladder, which looked normal and contained no stones. We encountered, however, some thin pus and thought we must find out where it came from. We could not ignore the fact that it was there, and we therefore proceeded in a systematic fashion to look over the intestine; about midway in the ileum, we encountered a tiny perforation, a foreign body — a chicken bone — lying quite close to it. It was easy to poke it through the hole it had made in the intestine. But, of course, one could never make that diagnosis beforehand without roentgenograms, and we had not bothered to have them made. We did examine the foreign body by x-ray afterward, however, and if we had had a film before operation we probably should have had a better lead. My next bet was Meckel's diverticulum, without any thought of foreign body.

The patient had no recollection of having swallowed the chicken bone, but this must have occurred several months before; without any question, the bone was responsible for some of her previous attacks, since it pricked here and there on the way down.

Dr. Mallory: Here is the postoperative x-ray film of the chicken bone. The patient made an extraordinarily quick and uneventful recovery, the chart becoming flat within two days, despite the obvious generalized peritonitis found at operation.

CASE 28222

Presentation of Case

A seventy-five-year-old woman was admitted to the hospital because of abdominal pain of several hours' duration.

She was in good health until early on the morning of entry, when she was awakened by moderately severe pain in the abdomen to the left of the umbilicus. She arose, and bathed, but the pain grew gradually much worse and extended all over the abdomen, going through to the back and around the ribs. There was no true chest pain, but there was costal-margin pain with deep inspiration. Following onset of the pain, the patient took only a few sips of water, which she vomited. There was but slight nausea, and no subsequent vomiting. A normal bowel movement occurred in the morning. A physician found abdominal tenderness, with pain coming in waves. He sent the patient to the hospital.

In the fifty years before entry, the patient had rare episodes of pain resembling the last attack. Three years before entry, she consulted a physician because of this. At this time, roentgenologic examination of the upper and lower gastrointes-

tinal tract yielded no diagnosis. Subsequent to this examination, one or two attacks of similar character occurred, going away after a few days. Occasionally, the patient experienced transient sharp pain in the lower lateral part of the left chest when frightened. She had had no dyspnea or ankle edema. Twenty years before entry, a diagnostic curettage was performed for bleeding.

Examination showed an elderly woman who complained of pain moving across her abdomen in horizontal waves from a point to the left of the umbilicus. The abdomen was quite rigid, with generalized tenderness, and was rather dull to percussion, although it was obviously distended. High-pitched peristaltic sounds were audible over apparently undilated portions of bowel at the time of passage of a wave of pain. The lung fields were clear. The heart was not enlarged, and there was a soft apical systolic murmur. The pupils were of pinpoint size.

The blood pressure was 170 systolic, 90 diastolic. The temperature was 97.5°F., the pulse 85, and the respirations 15.

Examination of the blood showed a white-cell count of 7400 with 93 per cent polymorphonuclears, and a red-cell count of 6,250,000 with 90 per cent hemoglobin. The urine was normal. The serum amylase was reported as elevated.

A roentgenogram of the abdomen showed elevation of the diaphragm and poor aeration of both lower-lung fields. There was no evidence of free air beneath the diaphragm. A dilated loop of bowel consistent with either ileum or sigmoid lay in the left lower quadrant. No other definitely dilated loops of bowel were apparent.

The patient was given venoclyses of glucose in physiologic saline solution and morphine sedation. In the next eighteen hours, the temperature and pulse rose steadily to terminal levels of 103°F. and 130 respectively. The abdominal distention increased, and the patient failed rapidly. Death occurred about twenty-six hours after onset of the illness.

Differential Diagnosis

Dr. Champ Lyons: The salient features of this case are the age of the patient and the catastrophic events that started in the left upper abdomen. Pain of sudden onset became progressively severe and radiated through to the back. Nausea and vomiting were present initially but soon disappeared. The pain was wavelike, and the abdomen was distended and spastic. The presence of mild shock is indicated by the subnormal temperature and probably by the elevated red-cell count. The life-endangering character of the difficulty is emphasized by the early death of the patient.

Gallstone colic and acute appendicitis with perforation are unlikely because of the onset of pain in the left abdomen. Rupture in an ectopic pregnancy is excluded by the age of the patient. Dissecting aortic aneurysm is an unlikely possibility with persistent urine formation. Three diagnoses must be seriously considered: perforation of a benign or malignant gastric lesion, high intestinal strangulation obstruction and acute pancreatic necrosis. The colicky pain, the absence of air under the diaphragm, the absence of gas in the jejunum, the character of the peristaltic sounds and the elevated serum amylase suggest that acute pancreatic necrosis is the proper diagnosis. The low leukocyte count and the history of previous rare attacks of similar pain are characteristic.

Acute pancreatic necrosis is hemorrhagic at its inception. If death follows after three or four days, the pathologist usually finds a gangrenous pancreas, and if the patient succumbs at a much later date, the pancreas may be suppurative. *Clostridium welchii* is frequently present on culture. I believe that this pancreas was hemorrhagic, with evidence of retroperitoneal dissection of serosanguineous exudate containing *Cl. welchii*.

The etiology of pancreatic necrosis is variable. The main factors are direct trauma, vascular injury, infection and bile invasion. Biliary-tract disease is concomitant in about 60 per cent of the patients, but there was no history of biliary colic in this patient, and a previous x-ray examination of the upper intestinal tract was reported negative. The onset of the pain was in the early morning and not after a full meal. Hence, bile reflux seems an unlikely cause of this pancreatic disorder, although the history of rare attacks of pain for fifty years is consistent with a biliary etiology. There is nothing to suggest a traumatic or infectious etiology. The patient's age indicates the existence of arteriosclerosis, and I believe that a vascular accident is the most likely cause of the acute pancreatic necrosis.

Dr. Allen G. Brailey: I should like to ask Dr. Lyons how he fits the presence of a dilated loop of bowel and cramplike peristalsis into this picture.

Dr. Lyons: We are not sure that the gas was not in the sigmoid, and this acute episode starting in the left upper abdomen ought to have produced high jejunal strangulation, not lower ileal obstruction.

Dr. Tracy B. Mallory: Why should the pain of pancreatitis be crampy, however?

Dr. Lyons: I do not know, but it is. There are two theories about it: one is that the celiac axis is involved in the inflammatory process, and the other is related to the persistent swelling of the capsule. I discount the capsule theory but am willing to accept the celiac-axis suggestion.

DR. RICHARD H. SWEET: It is very common to confuse the diagnosis of acute pancreatitis and acute small-bowel obstruction, and it is difficult to differentiate them. One point that I have always considered helpful is that the patients with pancreatitis have a steady, intense pain in the back.

DR. BENJAMIN CASTLEMAN: How about the white-cell count?

DR. LYONS: It is characteristically low in acute pancreatitis.

CLINICAL DIAGNOSIS

Acute pancreatitis?

DR. LYONS'S DIAGNOSES

Acute pancreatic necrosis, hemorrhagic, probably secondary to thrombosis or embolism of pancreas.
Peritonitis, acute (*Cl. welchii*).

ANATOMICAL DIAGNOSES

Acute hemorrhagic pancreatitis.
Cholecystitis, chronic.
Choledocholithiasis, probable.
Peritonitis, acute (*Cl. welchii*).
Thrombosis of splenic vein.
Pneumoperitoneum.
Pneumohydrothorax, bilateral.
Arteriosclerosis, aortic and coronary, marked.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Post-mortem examination did show acute hemorrhagic pancreatitis in the distal half of the pancreas. The process had involved the splenic vein, which showed complete but fresh thrombosis, and there was not as yet necrosis of the spleen. Dr. Lyons prophesied that we might well obtain a positive culture for *Cl. welchii*. There was more obvious evidence of *Cl. welchii* infection, since gas gushed from the peritoneal cavity on our primary incision, and the liver and the spleen and some of the other tissues were grossly crepitant.

So far as the etiology is concerned, we have nothing positive to contribute. The patient did, as most of these patients do, have severe biliary-tract disease. The gall bladder was small, firm and very fibrous, almost imbedded within the liver; it contained neither bile nor stones. The remaining biliary tract showed marked dilatation, with thickened walls and evidence of very long-standing chronic infection. Again, no stones were present in the ducts, but a small pigment stone that was found lying free in the duodenum may well have been squeezed out of the duct in our preliminary manipulations. Unquestionably, the patient had had severe infection of the biliary tract for several years. We did not make out any involvement of the celiac axis; she had moderate arteriosclerosis, which was not directly connected with this lesion.

DR. FLETCHER H. COLBY: Could the lesion have been due to bile reflux?

DR. LYONS: It is not likely that bile reflux caused the distal end of the pancreas to become necrotic.

DR. COLBY: How do you account for the *Cl. welchii*?

DR. LYONS: Dr. Lester Dragstedt* has written an article on the pancreas in which he emphasizes the fact that *Cl. welchii* is important in this whole problem. His evidence is very good from an experimental point of view, and I think perhaps we have not paid enough clinical attention to it. I do not believe that the Welch exotoxin, which is extremely hemolytic, could have been active in this woman, since she had a red-cell count of over 6,000,000. I do not believe it was toxemia, or that treatment with *Cl. welchii* antitoxin would have been worth while. I am inclined to believe that this toxemia was the result of some action of the Welch bacillus on the pancreatic cells or a result of some bacterial poison that is a chemical constituent of the Welch bacillus itself. We do not know what it is, but it is almost universally associated with pancreatitis.

DR. COLBY: Where does the Welch bacillus come from?

DR. LYONS: It is always in the intestinal tract.

*Dragstedt, L. R., Haymond, H. E., and Ellis, J. C. Pathogenesis of acute pancreatitis (acute pancreatic necrosis). *Arch. Surg.* 28:232-291, 1934

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REGULATION OF SALE OF BARBITURATES

A recent study[1] by a committee of the Connecticut State Medical Society gives ample proof of the conviction that the promiscuous use of barbiturates should be a matter of public concern and that these drugs should be sold only on prescription. That the same sentiment is held by the physicians in Massachusetts is evidenced by the fact that a recent legislative bill to limit the retail sale of barbituric acid, its derivatives and certain other sedatives to those possessing prescriptions from duly registered physicians, dentists and veterinarians was supported by the Massachusetts Medical Society. For this bill to be postponed to the next meeting of the General Court was unfortunate, particularly in view of favorable action on similar bills by the legislatures of certain other states; the sale of such drugs, however, is partially under federal control.

According to Section 502 (*f*) of the Federal Food, Drug and Cosmetic Act,[2] a drug is considered to be misbranded "unless its labeling bears adequate directions for use . . . ." However, since Section 502 (*j*) states that a drug shall be deemed to be misbranded "if it is dangerous to health when used in the dosage, or with the frequency or duration prescribed, recommended or suggested in the labeling thereof," and since the Food and Drug Administration[3] has stated as its opinion that the barbiturates are included among drug products that are too dangerous for indiscriminate use, even if sold with labeling attempting to give "adequate directions for use," most manufacturers are taking advantage of the exemption granted in the regulation of Section 502 (*f*) — namely, that the drug may be distributed if its label bears the statement, "Caution: To be used only by or on the prescription of a physician . . . ."

Hence, the inspectors of the Food and Drug Administration are empowered to report any interstate shipment of a barbiturate — "interstate shipment" is believed to exist until the product is in the hands of the consumer — that does not bear on its label the above statement, in addition to the statement, "Warning: May be habit forming," required by Section 502 (*d*). Obviously, a retail druggist who dispenses a barbiturate in a container that is not properly labeled may be prosecuted; furthermore, the broader interpretation of the regulations prohibits the sale, other than on prescription, of such drugs, even in containers that are not misbranded. For the past year, the federal inspectors have conducted cross-section investigations to determine the extent to which these requirements are being observed by the retail druggists, and although only one legal action has been brought on the basis of improper retail sales, further proceedings will be inaugurated if such sales continue. Of course, the Food and Drug Admin-

istration has no control over products manufactured and sold within Massachusetts.

At least some advance has been made toward prohibiting the over-the-counter sale of barbiturates, and the legislatures of all states should create statutes, conforming with the regulations of the Food, Drug and Cosmetic Act, that will completely eradicate the evil.

References

1. Committee on Drug Addiction, Connecticut State Medical Society. Barbiturate addiction. *Conn. State Med. Jour.* 6:124, 1942.
2. *Federal Food, Drug and Cosmetic Act and General Regulations for Its Enforcement.* Service and Regulatory Announcements (Food, Drug and Cosmetic No. 1), Food and Drug Administration, Department of Agriculture. Washington, D. C.: Government Printing Office, 1939.
3. Release by Food and Drug Administration, Federal Security Agency, dated April 24, 1941.

PULSE — AND THE FUTURE

With an ever-increasing percentage of recent medical graduates called to the colors, a correspondingly greater burden falls on those too old for active military service and on those still in that period of training without which they would be of little use — as physicians — either in civilian or in military life. The former group has had experience, dulled a little, perhaps, by advancing years, but it is on the younger men that much of the burden of the present war must necessarily fall, although too many of them seem unaware of this trenchant fact. Plans for and visions of the future should not and must not come entirely from the older group. No matter what the fortunes of the next few years, a new era is being opened up, of which the mainstay will patently be the youth of today: the medical student of 1942 is the army officer of tomorrow. It is but just and proper, therefore, that their views — whether right or wrong — be publicized in some material manner. Since this country is fighting for democracy, a democracy to fight for must exist.

Pulse, which is the official publication of the New England section of the Association of Internes and Medical Students, expresses the views of one portion of the medical youth of America, and there is reason to believe that there are nonmembers who hold similar views. Some, of course, do not agree; and hereon rests the responsibility of the editors of the publication: they must be rigorous in their efforts to represent truly the constituency under whose name they have chosen to promote themselves.

What are the purposes of this organization? It aims to serve the best interests of medical students and interns, wherever they may be, and to maintain and advance the ideals of the medical profession, thus serving society in general without respect to race, creed or color. More specifically, now that the United States is at war, this association aims to rally every medical student to an all-out war effort, to aid civilian defense by the training of Red Cross crews and catastrophe squads, to furnish, so far as possible, medical aid to the United Nations and to investigate what immediate changes might profitably be made in the curriculums of medical schools, so that these courses of study may be drawn more closely into line with the needs emerging from the present crisis. The members further wish to help in assuring that internships are of maximal educational value now that but one year is guaranteed and further training — except for service in the Army or Navy — is difficult to obtain.

In the April issue of *Pulse* appears an illuminating analysis of the financial needs of medical students under the new twelve-month medical-school system. One has, in a vague way, been aware that financial hardships must inevitably fall on some students under the new system, and although the constituted authorities are making every effort to avoid undue hardships, the average physician — who might be of help in one way or another — has not been apprised of the true state of affairs. The article is well worth study by all who are interested in the future of medicine.

Pulse is distributed as widely as circumstances permit among medical students, interns and physicians, and its columns are open to contributions as are those of any other periodical. Those who desire to obtain copies or to submit short articles should address their letters to 368 Longwood Avenue, Boston.

MEDICAL EPONYM

Parry's Disease

Sir William Osler considered that if any name should be attached to the syndrome of exophthalmic goiter, it should be that of Caleb Hillier Parry (1755–1822), M.D., F.R.S., whose description was published posthumously by his son in *Collections from the Unpublished Medical Writings of the Late Caleb Hillier Parry* (London, 1825: Vol. 2, p. 111). The condition is described under the general heading, "Diseases of the Heart":

> *Enlargement of the Thyroid Gland in Connection with Enlargement or Palpitation of the Heart.* There is one malady which I have in five years seen coincident with what appeared to be enlargement of the heart, and which, so far as I know, has not been noticed, in that connection, by medical writers. The malady to which I allude is enlargement of the thyroid-gland.

This introduction is followed by the report of 8 cases showing a thyroid tumor with symptoms of tachycardia, exophthalmos and edema (1 case), of 7 cases of swelling of the thyroid gland with tachycardia or palpitation and of 5 cases of thyroid enlargement without heart symptoms.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Case History: Fatal pernicious vomiting in pregnancy

A thirty-one-year-old primipara was sent to the hospital toward the end of the third month of pregnancy because of nausea and vomiting. The past history was irrelevant. Although the patient had been married sixteen years, this was her first pregnancy. Physical examination showed no abnormalities other than moderate dehydration and a pulse elevated to 100. The nausea began about the sixth week, and treatment at home had been instituted; since the patient did not improve, she was hospitalized. Administration of insulin, glucose, adrenocortical extract and transfusions resulted in marked improvement for a few days, and she was sent home. Ten days later, she returned to the hospital in extremis and died without surgical intervention.

Autopsy showed acute parenchymatous nephritis, acute degenerative hepatitis, congestion of the spleen and early degeneration of the adrenal glands.

Comment. Pernicious vomiting, and this was a true case of pernicious vomiting, should not result in death. The patient should have been hospitalized earlier. The treatment at the hospital did result in improvement, but it was probably not sufficient to warrant discharge.

The modern treatment of pernicious vomiting in pregnancy consists of hospitalization, the cessation of all food by mouth for forty-eight hours, the use of intramuscular thiamine chloride and intravenous glucose, and sedation. If this treatment is begun before definite degenerative disease has developed, improvement is rapid and remarkable. Rarely do such cases reach the point where therapeutic abortion is indicated to save life. This patient did not have thiamine chloride, but she did have glucose and transfusions. It is very probable that religious beliefs prevented surgery.

There is no such thing as pernicious vomiting per se in pregnancy. Death in these cases is due to pure starvation, which results in acidosis and degenerative changes in the kidney and liver.

One cannot help believing that this death was entirely avoidable. Earlier hospitalization and the routine treatment would probably have resulted in recovery. Therapeutic abortion was apparently not considered. Patients not treated early enough may need therapeutic abortion to prevent death, but this procedure, when a case has been intelligently handled and hospitalized early, is practically never necessary.

DEATHS

DELAHANTY — William J. Delahanty, M.D., of Worcester, died May 10. He was in his eighty-fifth year.

A native of Fitchburg, Dr. Delahanty received his degree from Dartmouth Medical School in 1883. He was an incorporator and a member of the staff of St. Vincent's Hospital, and was on the staff of the Worcester City Hospital for more than fifty years. He was a trustee of the Worcester State Hospital, and was a fellow of the Massachusetts Medical Society and the American Medical Association.

FIELD — Henry M. Field, M.D., of Norwood, died May 20. He was in his sixty-eighth year.

Dr. Field received his degree from Harvard Medical School in 1904. He was a member of the staff of the Norwood Hospital, and a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

O'LEARY — Cornelius J. O'Leary, M.D., of Brighton, died May 20. He was in his fortieth year.

Born in Charlestown, Dr. O'Leary received his degree from Tufts College Medical School in 1933. He had been associate medical examiner for the northern district of Suffolk County for seven years and was a fellow of the American College of Surgeons, the Massachusetts Medical Society and the American Medical Association.

His widow and four children survive him.

WAR ACTIVITIES

CIVILIAN DEFENSE

New Publications

Protection of Hospitals, Bulletin No. 3 of the Medical Division of the United States Office of Civilian Defense, prepared in collaboration with a special committee of the American Hospital Association, has now come from the press in its official form. It was previously published in several hospital journals in order that the material could be used by hospitals at the earliest possible moment.

The bulletin discusses protection of hospitals against air raids under the following heads: protection of building fabric, patients and personnel; protection of glass; ventilation; protection against fire; rescue squads; air-raid shelters; blackout regulations; protection of utilities; facilities for care of casualties; unit system and reserve stocks; the ambulance entrance; morals; distribution of casualties to wards.

Diagrams show how sandbag barricades can be used for temporary reinforcement, how to protect windows against shattering of the glass without cutting off ventilation, and several methods of blacking out. There is a sketch suggesting how an ambulance entrance can be designed to eliminate unnecessary turns, and there are also designs for signs to guide ambulances in the blackout.

The section on protection of glass gives detailed instructions on materials that can be used and methods of applying them. Under "Protection against Fires," there is a description of the various types of incendiary bombs and of the approved methods of fighting them. The report emphasizes the importance of fire and evacuation drills.

Facilities especially needed for the care of war casualties are a special reception room, in which casualties may be examined to determine their condition and immediate treatment, operating rooms in protected parts of the hospital (lower floors or basement), decontamination station for gas casualties and ample provision for a mortuary.

Volunteers in Health, Medical Care and Nursing has been issued for use of executives in civilian defense volunteer offices and of executives of agencies using volunteer services in these fields. The pamphlet outlines qualifications and duties for the following activities: automobile drivers, blood donors, child-care assistants, first-aid teachers, home-nursing teachers, health-department assistants, hospital and clinic assistants, laboratory assistants, library assistants, medical social-service assistants, nurses' aides, nutritionist assistants, occupational-therapy assistants, physiotherapy assistants and sanitation assistants.

MISCELLANY

DANGERS OF INDIRECT CONTACT WITH TUBERCULOUS PATIENTS

As long ago as 1865, Villemin successfully passed the "virus" of tuberculosis from one animal to another. Twelve years later (five years before Koch's discovery of the tubercle bacillus), von Tappeiner caused dogs to develop tuberculosis by allowing them to inhale sputum from a consumptive patient. Although direct lip contact is today considered the most potent means of transferring tubercle bacilli from person to person, knowledge of the relative dangers of indirect contact with tuberculous lungs and their secretions is still incomplete. Three recently published papers give evidence of this and, at the same time, sharpen one's perception of the manner in which bacilli go from host to victim.

The Occurrence of Tubercle Bacilli on Books and Garments Handled by Patients with Open Tuberculosis

(Jacobs, M. A., and Petroff, S. A. *Quarterly Bull. Sea View Hosp.* 7:33–39, 1941.)

Books read by tuberculous patients probably are occasionally contaminated by sputum in the form of droplets expelled during coughing or speaking as the book is closely held to the face or at such a level that any droplets expelled may readily be deposited upon the paper. Also, they may contaminate books by licking the thumb or finger when turning the pages. Transmission of infection to a second reader appears likeliest to occur when the recipient with moist thumb or finger handles the contaminated pages, supposedly harboring the bacilli.

There is a general agreement that large portions of the bacilli deposited on the pages become dry and nonviable after a short time. Kenwood and Dowe exposed papers to coughing patients and dried them for one month, after which the washings from the paper surfaces were inoculated into guinea pigs of which not a single animal developed tuberculosis. Other experiments of this kind point to the conclusion that although the risk of infection from books is not to be belittled, the possibility of transmission from such channels is extremely small.

Jacobs and Petroff permitted certain patients with advanced pulmonary tuberculosis, with uncontrollable cough and with sputum of Gaffky 6 to 8, to handle books as carelessly as possible. They coughed on the marked pages, and wet their thumbs with saliva when turning these pages. Scrapings later derived from the marked pages were collected and suspended in physiologic saline solution. Tuberculin-negative guinea pigs were inoculated with this solution. Three of the 16 guinea pigs died from intercurrent disease, and no evidence of tuberculosis could be found at post-mortem examination. The other 13 remained tuberculin negative ninety-two days after the inoculation, when they were sacrificed.

Another set of experiments demonstrated that the dust collected by scrapings from garments worn by patients with open tuberculosis did not infect guinea pigs. However, this failure should not give rise to a sense of false security and to a laxity of precautionary measures. The summary includes the following suggestions:

At present, the best way to ease the mind of the possibility of transmission by a book that has been handled by a patient with open tuberculosis is to store or quarantine the book for several weeks until the morbid material has completely dried, since it has been shown repeatedly that the drying robs the bacilli of their power of producing disease in animals. This measure was recommended by the British Joint Tuberculosis Commission.

There is no suggestion of importance concerning how the patients' garments should be disinfected. Perhaps the safest way is to expose them to the sun and air for a few days before storing them away.

Survival of Tubercle Bacilli

(Smith, C. R. *Am. Rev. Tuberc.* 45:334–345, 1942.)

Cultures were made from swabbings of bedside tables, lamps, bed frames and other articles in rooms occupied by patients at Barlow Sanatorium, and from room dust, sweepings and cotton filters through which room air had been sucked. Uniformly negative results led to speculation regarding the effect of daytime roomlight on living tubercle bacilli.

Review of the literature seems to sustain the statement

of Park and Williams that: "Tubercle bacilli in sputum when exposed to direct sunlight are killed in from a few minutes to several hours according to the thickness of the layer and the season of the year. They are usually destroyed by diffuse daylight in from five to ten days. Dried sputum in rooms protected from abundant light has occasionally been found to contain virulent tubercle bacilli for as long as ten months."

For the present experiment, suspensions of virulent human tubercle bacilli in water or in sputum were spread on cover slips in 0.05-cc. amounts and allowed to dry. Some of these preparations were placed in a small unheated room in the light of an unglazed but screened north window through which the sun was known never to shine; others were kept in complete darkness within a cardboard box inside a second such box, which in turn was kept in a table drawer of an unheated room. This was done during a clear, dry period in midwinter at Los Angeles.

A second set of tests was run in the early spring during cloudy and rainy weather, and a third set of tests in midsummer. The following winter, viability was also tested in the electric refrigerator.

The viability of tubercle bacilli was determined by animal inoculation and by culture.

Dried tubercle bacilli survived unfiltered north roomlight from four hours to five days under varying conditions. They were nonviable, according to the methods of recovery used, at one to twelve days; the viability was not established in one case.

Viability in the dark was from less than forty days to between three and a half and five months.

Viability in the refrigerator was between six and a half and fourteen months.

Tubercle bacilli were more readily recoverable and after longer periods of exposure when the dose deposited was larger. They lived longer in smears made from sputum than in those from water suspensions. They lived longer in the winter than in the spring and summer.

Variations in relative humidity and periods of partial cloudiness had no effect on viability.

Unfiltered daytime roomlight probably plays a very important role in preventing cross-infection and in protecting the employees of tuberculosis sanatoriums.

THE DISSEMINATION OF TUBERCLE BACILLI FROM FRESH AUTOPSY MATERIAL

(Sloan, R. A. *New York State J. Med.* **42**:133, 1942.)

Two incidents seem to have prompted this study: the isolation of acid-fast organisms from the surface of eyeglasses worn during an autopsy on an active case of tuberculosis; and the observation that the incidence of tuberculosis among medical students appears to be proportional to their contact with autopsy material during the second year in medical school. The compression of the crepitant lung, causing expulsion of minute amounts of bacterial-laden air, might simulate a human cough and thus be responsible for the dissemination of bacteria.

Lungs from patients who died from tuberculosis were sectioned in the usual manner, the trachea was opened, regional lymph nodes were examined, and all cavities were opened with scissors. This was done under a shield, equipped with a glass plate situated about 20 cm. directly above the specimen. After a fifteen-minute examining period, the plate was washed with sterile saline solution.

The growths obtained from the washings led to the conclusion that methods of examination that make use of a compression technic contaminate the atmosphere in the vicinity of the autopsy, and that fresh tuberculous lungs are decidedly dangerous and are a potent source of atmospheric contamination, against which methods of proper protection should be devised. — Reprinted from *Tuberculosis Abstracts*, May, 1942.

NOTES

Seven appointments to the teaching and research staffs of the Harvard Medical and Dental schools were recently announced by Harvard University as follows: John B. Hazard, M.D. Harvard '30, of Wellesley, assistant in pathology; Mark S. Donovan, M.D. University of Michigan '35, of Boston, assistant in roentgenology; Luke Gillespie, M.D. Harvard '37, of Winthrop, assistant in obstetrics; Dario Azevedo, M.D. Faculty of Medicine, of Lima, Peru, '30, research fellow in physiology; Zenal Kiper, M.P.H. Harvard '40, of Boston, research fellow in surgery; Francis Rouillard, M.D. Harvard '27, of Cambridge, assistant in obstetrics; and Richard D. Garrett, D.M.D. Harvard '39, of Glens Falls, New York, assistant in surgery.

Harvard University has recently announced the appointment of J. Howard Mueller, Ph.D., as professor of bacteriology and immunology at Harvard Medical School and School of Hygiene and Public Health, a position made vacant by the death of Dr. Hans Zinsser in September, 1940. Drs. Fuller Albright, Allan M. Butler and Hiram H. Merritt were promoted to associate professorships in medicine, pediatrics and neurology, respectively, and Dr. Frederick J. Stare, a graduate of the University of Chicago School of Medicine, was named assistant professor of nutrition.

At a recent meeting of the American Association of the History of Medicine, the William Osler Medal was awarded to John T. Barrett, '43, of Boston University School of Medicine.

Dr. Leopold F. King, of Lowell, was recently elected president of the Massachusetts Society of Examining Physicians. He succeeds Dr. Roger T. Doyle.

Dr. Walter B. Cannon, George Higginson Professor of Physiology at Harvard Medical School, has recently been made an honorary member of the Russian Academy of Sciences. Two other Americans and two Englishmen were similarly honored, this being the first time since the Russian revolution that such distinction has been granted to foreigners.

REPORTS OF MEETINGS

CARNEY HOSPITAL JOURNAL CLUB

At a regular monthly meeting of the Carney Hospital Journal Club at the hospital on January 8, Dr. Robert Wilkins, of the Evans Memorial Hospital, spoke on "Recent Developments in the Pathological Physiology of Hypertension." After briefly reviewing the fundamental work of Goldblatt, on which most experimental investigation in this field is now based, Dr. Wilkins discussed the types and characteristics of experimentally produced hypertension. The first general type is popularly known as that caused by "renal ischemia." This was originally effected by Goldblatt by applying a clamp on the renal artery and was later produced by the artificial constrictive perinephritis of Page's cellophane capsules. That any changes in such cases are not truly the result of anoxia of the kidney is now generally accepted, since experiments have

demonstrated that there is no decrease in the blood flow to such an organ. The significant change is apparently one from a pulsating to a steady type of blood flow.

The following facts are characteristic of such hypertension. It is cured by removal of the involved kidney. The blood pressure may not immediately return to normal, apparently depending on the duration and degree of the hypertension. This is probably associated with its effect on the other kidney. Wilson and his co-workers have shown that the clamp keeps the elevated blood pressure from affecting that kidney, whereas the normal organ is adversely affected. Hypertension is increased if the normal kidney is removed; this indicates that the latter in some manner protects the animal. The onset of hypertension is not prevented, nor is its course altered by renal denervation, complete sympathectomy or pithing; this type of experimental hypertension has no relation to renal innervation and is probably humoral in its mechanism.

The second general type of experimental hypertension is the so-called "neurogenic" kind, which is produced by removal of the carotid sinuses and the depressor nerves (Heyman's operation) or by artificial increase of the intracranial pressure (Cushing). The characteristics of this type are its lability, its abolition by pithing or complete sympathectomy, and its failure to be eliminated if only the renal (adrenal) or the cardiac innervation is intact. This, then, is essentially a nervous mechanism as compared with the humoral character of the other type.

The relation of such hypertension to the human form is borne out by the fact that at least certain cases in man seem to have some degree of "renal ischemia." Furthermore, splanchnic sympathectomy has a definitely beneficial effect in certain cases. And since this operation removes both the renal and adrenal innervation, it is conceivable that the kidney is a common factor. In further support of this hypothesis are the observations that in hypertensive patients there is a vasoconstriction of the efferent renal arterioles, as demonstrated by Smith's Diodrast-clearance and inulin-clearance tests, and that the blood of such patients is more vasoconstrictive than that from normal controls (Page).

Another problem is the character of "renin," a substance that is obtained from kidneys and is the precursor of angiotonin and hypertensin, which are now being employed to produce experimental hypertension. Earlier preparations of this compound were apparently impure, for they caused a depressor effect after the pressor. It has now been demonstrated that this substance is a protein, is heat labile, and combines with a pseudoglobulin to produce angiotonin, the last reaction being dependent on the temperature, the time and the proportion of reacting substances. All these are, of course, characteristics of an enzyme. Angiotonin (hypertensin), on the other hand, is a protein that is heat stabile, dializable and crystallizable, and is destroyed by an excess of renin or tissue extracts. Therefore, it is a relatively pure substance but is not an enzyme.

The crucial experiment attempted by Dr. Wilkins and his co-workers was to determine whether angiotonin causes human hypertension of the proper pattern. For this purpose, they used themselves as subjects and employed angiotonin supplied by Page. It was concluded that this substance does cause a characteristic and marked hypertension, without any significant side effects, in the majority of subjects. There is often dizziness at the onset, and some subjects later experienced substernal oppression and palpitation. One doctor complained of severe headache closely resembling that of hypertension. This indicates that these symptoms, so often clinically attributed to a superimposed "neurosis," are in reality the result of the high blood pressure. There was a significant rise in the blood pressure (190 systolic, 120 diastolic). Bradycardia, a constant finding, could be abolished by atropine, whereas the hypertension was heightened. The venous pressure, surprisingly, rose to failure levels, with visible neck veins in certain cases. There was a concomitant decrease in vital capacity. The cardiac output, as suggested by Starr, was sharply diminished. This is the only pressor substance that acts in this way, according to this observer, who has reported that adrenalin, amphetamine (Benzedrine) and so forth either do not change the output appreciably or increase it. These findings suggested the similarity to cardiac failure, and this was borne out further by teleoroentgenograms and chest plates, which revealed increased lung markings or enlargement of the cardiac shadow, or both. That there is peripheral vasoconstriction was corroborated by skin temperatures and plethismographs. That angiotonin is a true vasoconstrictor independent of the sympathetic nervous system was proved by its action in the absence of this system and when injected intra-arterially and at skin temperature to the part measured. It does not overcome sympathetic control, however. Whether the hypertension resulting from angiotonin is the same as the naturally occurring disease depends on how one wants to interpret the evidence, for there are some facts in favor of both views. The lack of any increase in venous pressure in the human disease, unless there is cardiac failure, is in contrast to the experimental facts, but the cardiac failure is an acute episode. The spasm of the renal efferent arterioles is found in both conditions. Page and Houssay both hold the opinion that the substance causing human hypertension is either similar to or the same as angiotonin (hypertensin).

Since the presence of a normal kidney acts as a protection against both types of hypertension, there have been numerous attempts to find depressor substances in normal kidneys to counteract the pressor material from abnormal renal tissue. Such depressors act only if there is a high blood pressure. In all the outstanding laboratories, there are now such materials, which decrease the hypertension in animals and in certain human subjects. Since there are many severe reactions at first, Page has so far employed his depressor only in very advanced cases and in practically moribund patients. Nevertheless, he is firmly convinced that he is gradually obtaining a purer substance and that the reduction of blood pressure is not attributable to the side reactions of shock, fever or toxic manifestations, as some observers maintain. In favor of his contention is the slow and prolonged reduction of blood pressure, in contrast to the precipitous fall in toxic reactions and shock. Furthermore, there have been satisfactory results in some patients without side reactions, whereas some of those with the severest toxic manifestations revealed no fall in pressure. The hypertension returns if this therapy is not continued. All the measurable signs, such as increased cardiac output, decreased venous pressure and efferent arteriolar dilatation, testify to the efficacy of this "antiangiotonin."

Schroeder, in New York, working from the chemical standpoint that all these compounds have the basic structure of tyrosinase, has used this substance to render angiotonin inactive in vitro. It definitely decreases the hypertension in experimental rats, but its use in human beings is not advocated. It was advanced as a method of investigation, and is too difficult technically to be used in man.

Another form of therapy of human hypertension that has met with success in some cases in the hands of certain

surgeons, such as Peet and Smithwick, is sympathectomy. The question arises whether it is merely palliative and nonspecific, but there is no doubt of its efficacy in properly selected cases. It should be noted that there is no measurable increase of renal blood flow after this operation. In considering human hypertension in general, one should realize that it is not a simple problem, for apparently civilization adds some conditioning factor, as evidenced by the lack of this syndrome in the Australian aborigines and in Negroes in their native African countries. Whether this indicates the presence of a neurogenic factor is still a moot point.

In answer to questions, Dr. Wilkins pointed out that such therapy as might result from the introduction of angiotonin inhibitors will probably have to be periodic and continuous like insulin. In certain cases in which a cycle is present, it might be possible to break in and thus allow smaller doses or less frequent administration of the material. The strong heredity factor and neurogenic pattern in human hypertension are corroborated by pressor tests of any type (immersion of hands in cold water), which demonstrate that hypertensive patients show a stronger reaction and that there is a higher percentage of future hypertensive patients in present hyper-reactors and their children than in those showing a normal response.

NEW ENGLAND PATHOLOGICAL SOCIETY

A regular meeting of the New England Pathological Society was held on January 15 at the Evans Memorial, Massachusetts Memorial Hospitals. Dr. B. Earle Clark presided.

The first paper, "Experimental Allergic Inflammation of the Intestine," was presented by Dr. George Hartley. Previous work suggested that ingested antigen is localized in the intestinal wall by specific antibodies. Because the work of Opie and others has shown that allergic inflammation in the skin (the Arthus phenomenon) is caused by a localization of antigen by antibodies, the demonstration of such a reaction in the intestine would prove that antigen is localized by antibodies in this organ. Following the injection of crystalline egg albumen into the tied-off cecum or directly into the wall of the cecum of hypersensitive rabbits, a severe inflammatory reaction developed locally. A similar inflammatory response was produced in the ileum of hypersensitive rabbits following the injection of antigen into a small radicle of the mesenteric artery. The inflammation was characterized by a marked neutrophilic infiltration of the entire wall (mucosa, submucosa, muscularis and serosa), edema and slight hemorrhage of the submucosa, and vascular congestion of the submucosa and subserosa. Eosinophils in rabbits are difficult to distinguish from neutrophils, but Dr. Hartley believes that there was an infiltration of these cells, as well as of the neutrophils, in the intestinal wall. At the site of the mesenteric arterial injections, acute arteritis and periarteritis developed. No lesions were present in the normal control rabbits that were treated in the same manner as the hypersensitive animals. All the lesions were present after twenty-four hours. Older lesions have not yet been studied. These experiments demonstrate for the first time the direct production of allergic ileitis. The resemblance of this allergic inflammation of the intestine in rabbits to acute appendicitis and the nonspecific inflammations of the small intestine in human beings suggest the possibility that some of these inflammatory reactions may be allergic. Finally, since it has been definitely established that allergic inflammation in the skin (the Arthus phenomenon) is the result of the localization of antigen by antibodies, these experiments suggest that antigen is localized by specific antibodies in the intestinal wall.

In the discussion, it was questioned whether Dr. Hartley had justified his conclusions. The fact that the histologic preparations of his experimental animals resembled appendicitis and ileitis was insufficient to prove that these diseases are allergic. Dr. Alan Moritz warned against giving too much emphasis to the eosinophil as evidence of an allergic state.

The next paper, "Temporal Arteritis: Report of a case," was presented by Dr. David Skinner. Biopsy of one temporal artery showed moderate thickening of all the coats, with preservation of the internal elastic membrane. The adventitia and portions of the media were replaced by old granulation tissue. The adventitia, media and intima were heavily infiltrated with endothelials, lymphocytes, occasional plasma cells and very rare eosinophils, but no giant cells were observed.

In the discussion, Dr. Tracy B. Mallory reported that he had seen 6 cases at the Massachusetts General Hospital. He brought out the point that the vessel changes can usually be distinguished from periarteritis nodosa microscopically, but that occasional difficulty may be encountered in differentiating it from thromboangiitis obliterans.

Another paper, "Spontaneous Renal Infarction in Infants," was presented by Dr. Skinner. During the last fourteen years, 8 cases of renal infarction have been observed among 462 consecutive autopsies on infants one year old or younger, exclusive of stillbirths. The infarct was bilateral in 2 cases, total in 4, and partial in 2. Venous thrombi were present in 3 cases. Associated conditions were pneumonia in 5 cases, cleft palate with malnutrition in 2, acute enteritis in 2, and marasmus in 2. No definite cause for the infarction could be determined. The next paper, "Wilson's Disease: Report of a case," was presented by Dr. Donald Nickerson. A twenty-five-year-old woman was admitted to the hospital complaining of enlargement of the abdomen and pain in the left upper quadrant. The patient had been perfectly well until the age of fifteen, when she began to have irregularity of the menstrual periods, followed by complete amenorrhea nine years later. On examination, the outstanding finding was a very large spleen, which reached to the crest of the ilium, and a painful subcutaneous nodule just above the umbilicus. Neurologic examination showed no definite spasticity but a coarse shaking tremor of both hands, hyperactive knee and ankle jerks, no interference with sensorium and evidence suggesting cerebellar dysfunction. Laboratory examination showed a rather marked secondary anemia, with moderate achromia and poikilocytosis. Blood chemical studies, including cholesterol, calcium, phosphorus, phosphatase and total protein, were essentially negative. The sedimentation rate was moderately active. The spinal-fluid examination, blood and spinal-fluid serologic findings, blood fragility studies and repeated Bence–Jones determinations on the urine were all negative. X-ray examination showed marked splenomegaly and moderate demineralization of the skeleton. The patient, who was discharged from the hospital with a diagnosis of Wilson's disease, progressed fairly well for nine months, during which time she had been studied in a Boston hospital, where the same diagnosis was made. The last admission was due to marked abdominal enlargement, with edema of the ankles, for which paracenteses were done; on the sixth hospital day a fatal hemorrhage into the intestinal tract occurred. Post-mortem examination showed an extreme cirrhosis of the liver, which weighed 675 gm. and whose gross and

microscopic appearance was that of a healed acute yellow atrophy. The spleen was markedly enlarged, weighing 740 gm., and showed no gross lesion beyond extreme engorgement. There was a small, perforated, esophageal varix from which a fatal hemorrhage had occurred. Examination of the brain showed distortion of the relation of the left basal ganglia, and microscopic sections showed rather extensive gliosis in the left lenticular area.

In the discussion, Dr. Ernst E. Mathias suggested that Wilson's disease may be one of a group of diseases, the other members being Huntington's chorea, pseudosclerosis and athetosis.

The final paper, "The Mitotic Activity of a Group of Colchicine-like Compounds," was presented by Dr. Charles Branch. It has been established that colchicine is a toxic drug that has a profound effect on cell division. Several investigators have attempted to find a substitute or derivative of comparable activity but less toxicity. The present study was concerned with a group of twelve such compounds, tested for their effect on mitotic activity. For each experiment, 50 mice (Strain C57), planted with sarcoma (Strain 37), were used. The compound to be tested was injected in varying doses, and the mice were sacrificed at regular intervals, up to twenty-four hours. Compounds differing considerably in their chemical structure all produced mitotic showers comparable to colchicine, but were apparently less toxic than that drug. Several of the animals with varying sized tumors were displayed.

BOOK REVIEWS

School Health Services: A study of the programs developed by the Health Department in six Tennessee counties. By W. Frank Walker, Dr.P.H., and Carolina R. Randolph. 8°, cloth, 197 pp., with 139 tables and 12 charts. New York: The Commonwealth Fund, 1941. $1.50.

In view of the steady growth of school health services in this country and the relatively important place they occupy in the public-health program, a critical study of objectives and the results obtained is long overdue. The authors have attempted such a study in a group of Tennessee counties where school health work has been well organized for ten years, and where uniformity of both examinations made and records kept far exceeds the average.

The main objective is the appraisal of certain standard procedures in terms of pupil response. The dominant influence of the presence of the parent at the time of examination comes as no surprise. Nursing supervision alone had much less influence in securing the correction of defects, but was far from negligible. Although preschool health supervision definitely increased the percentage of immunization of children against diphtheria and typhoid fever, it showed no effect on the percentage vaccinated against smallpox. A satisfactory response in all three kinds of immunization followed school supervision.

Some of the questions raised by this study are perhaps more significant than the conclusions that could be drawn. How far can routine school examinations go without interfering with more productive activities in the public-health program, or even with the correction of defects found? One might also ask how far a health department should go with school procedures that involve personal rather than public health. In terms of results, are routine dental examinations justified unless the community can provide corrective treatment when needed?

The authors' clear style and concise statement will appeal to the general reader, and the public-health worker will find in the book a challenge to more objective thinking in a somewhat nebulous field. The printing and format of the book uphold the usual high standard of the Commonwealth Fund publications.

A History of Medical Psychology. By Gregory Zilboorg, M.D., in collaboration with George W. Henry, M.D. 8°, cloth, 606 pp., with 21 illustrations. New York: W. W. Norton and Company, Incorporated. $5.00.

Nobody in America writes with more fluency than Gregory Zilboorg. As a leader in medical thinking he has brought to this country the best of the European tradition. This new volume on the history of medical psychology is not merely an account of what has happened but also a critical appraisal, intelligently organized and interestingly told. Up to the present time, no book more scholarly than this has appeared in English. How Dr. Zilboorg has been able to do it in the midst of his heavy work as a psychiatrist and psychoanalyst is explained in part by the fact that he has had the assistance of Dr. George W. Henry.

Although Dr. Zilboorg is himself a psychoanalyst, it cannot be said that this book suffers from psychoanalytic bias. It is written from the philosophic and humanitarian point of view. Only a physician with broad human contacts and vast learning could have produced this document, on which every physician can afford to look with pride.

This book is not for light reading, although there are many parts of it that are charming and amusing. Rather, it is a book for study and reference. It is a book one could keep on one's bedroom reading table, where in quiet and in reflection one could appreciate the scope and profundity of Dr. Zilboorg's labors.

Dr. Zilboorg points out several important facts that until now have not been adequately stressed. His emphasis on the neuroses (Chapter 9) and on "psychiatric revolutions" (Chapters 7 and 11) will guarantee the reader ample reward for reading these sections if he has not time to read the whole book.

Dr. Henry's separate contribution on mental hospitals (Chapter 14) is well worth reading, since the facts it contains should be common knowledge to every physician in America today.

About Ourselves: A survey of human nature from the zoological viewpoint. By James G. Needham, M.S., Ph.D. 4°, cloth, 276 pp., with 45 illustrations. Lancaster, Pennsylvania: The Jaques Cattell Press, 1941. $3.00.

The complex story of the development of animals and man is retold in a simple, often humorous, way by the former professor of entomology at Cornell University. There are chapters on the primates, man's remote ancestry, the development of the nervous system, instinct, learning, infancy and similar topics. The material is presented in language that a young adult could understand; this is an oft-repeated story, but well done, as might be expected from a well-trained biologist.

The last half of the book deals with a larger problem — society in its biologic aspects. Here one touches medicine, government, war, folkways, social behavior and human affairs. One senses that the author is not so happy in this broader field; certainly, his knowledge of medicine leaves much to be desired. For example, he gives eight symptoms of hysteria, no one of which would be accepted by a physician as diagnostically significant (page 216).

It is difficult for the reviewer to decide for whom this book was written. A grade school or college underclassman might profit by Part 1; Part 2, for adults, seems of less value.